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MANAGING COMMITTEE

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BUREAU OF HYGIENE AND TROPICAL DISEASES,  
Keppel Street, W C 1

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1948 { Date

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## BUREAU OF HYGIENE AND TROPICAL DISEASES

TROPICAL DISEASES  
BULLETIN

Vol 45]

1948

[No 1

## SLEEPING SICKNESS IN TANGANYIKA TERRITORY, 1922-1946

By H FAIRBAIRN, O B E , M D , D T M & H  
*Sleeping Sickness Officer, Tanganyika Territory*

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1 *Historical*

The epidemic of *T. gambiense* sleeping sickness which occurred in Uganda in the early years of the present century gradually spread down both sides of Lake Victoria and invaded German East Africa (now Tanganyika Territory). In 1907, the Germans established sleeping sickness camps at Kigarama, on the west shore of Lake Victoria just south of the Uganda border, and at Shirati on the east side, near the Kenya border [*Sleeping Sickness Bulletin*, 1909, v 1, 243]. In 1908, cases of sleeping sickness were discovered on Ukerewe Island, at the south of the Lake, and on the Islands of Bumbire and Iroba near the eastern shore and on the mainland of Ihangiro opposite to them [*ibid*, 396]. On Lake Victoria the Germans recorded 1,405 cases, of sleeping sickness in 1908-9, and 27 cases in 1912-13 (MACLEAN, 1927).

By extensive bush clearing, particularly along the River Mori, south of Shirati [*Sleeping Sickness Bulletin*, 1912, v 4, 244], they appear to have eliminated the tsetse fly and stopped the southward spread of the disease. It was while working in the River Mori area that KLEINE (1909) discovered the cyclical transmission of *T. gambiense* by *Glossina palpalis*.

*Lake Tanganyika*—Sleeping sickness reached the western (Congo) shore of Lake Tanganyika about 1901 and soon reached the eastern (German) shore, where it quickly spread. The Germans remarked that numbers of Africans,

bearers of trypanosomes, came from the Belgian Congo to German territory in one caravan of sixteen, ten persons were found to be infected [*Sleeping Sickness Bulletin* 1908 v 1 398].

By 1907 the authorities had established a sleeping sickness camp at Ntansa at the north end of the Lake and they recorded the disease as being present in the northern third of the Lake shore from Usumbura to the River Malagarasi [*ibid.*, 243]. In October 1908 1,517 patients were under treatment [*ibid.*, 396] but this number apparently included the Lake Victoria cases as well. Extensive clearings were undertaken, as in the Lake Victoria area.

By 1914 the Germans had had complete success in combating the disease in the Lake Victoria region, but they considered that the most widespread and most dangerous seat of infection was the Lake Tanganyika coast. The principal efforts of the Government were directed towards preventing the introduction of fresh cases, controlling native traffic, and clearing bush. No Africans from German East Africa were allowed to act as porters in the Belgian Congo [*this Bulletin*, 1914 v 3, 527].

It was while working at Ntansa that TAUTZ in 1911 showed that *G. morsitans* could transmit trypanosomes cyclically [*Sleeping Sickness Bulletin* 1911 v 3 291], an observation shortly afterwards published independently by KINGDON [*ibid.*, 391].

MACLEAN (1927) stated that in 1912-13 there were 3,303 cases under observation, but that most of these were from Ruanda-Urundi, now Belgian Mandated Territory (the northern part of Lake Tanganyika). He stated further that cases were found at the Malagarasi Delta by the Belgian authorities during their occupation of Kigoma and Western Ufipa between 1918 and 1921 but that no records were available and the numbers were not known.

*South-Eastern Fly-Block.*—In 1911 a focus of human trypanosomiasis was discovered on the upper reaches of the River Rovuma in the Songea District [*Sleeping Sickness Bulletin* 1912, v 4 200]. LAMBORN and HOWAT (1906) give a fuller account of this. They quote from an unpublished report by a German, Dr Woll (this is, possibly the Dr Woll cited to by Swynnerton, 1923) that early in 1910 an African was found ill with trypanosomiasis. He had come from his village at the junction of the upper Rovuma and Sawasaru (? Sasawaru) rivers. After this patient had been discovered, numerous cases of the same disease occurred along the route on which it was definitely ascertained, he had travelled. In 1911 a segregation camp was established at Sawasaru to deal with the outbreak, and between 1911 and 1913 seventy-two cases were isolated. From this area the disease spread northwards, and in 1917 it had reached the hinterland of Kilwa, having crossed the River Mbemkuru. TAUTZ and HUMER (quoted by SWYNNERTON 1923) stated that the foci of human trypanosomiasis behind Kilwa and Lindi and further south were confined to water-holes and the banks of rivers that were the halting places for Yao labourers passing from the southern infected foci to the Lindi-Kilwa plantations, and that cases did not occur in the surrounding country. TAUTZ in 1913 established that the disease in this area was due to *T. rhodesiensis* [*this Bulletin* 1913 v 1 513].

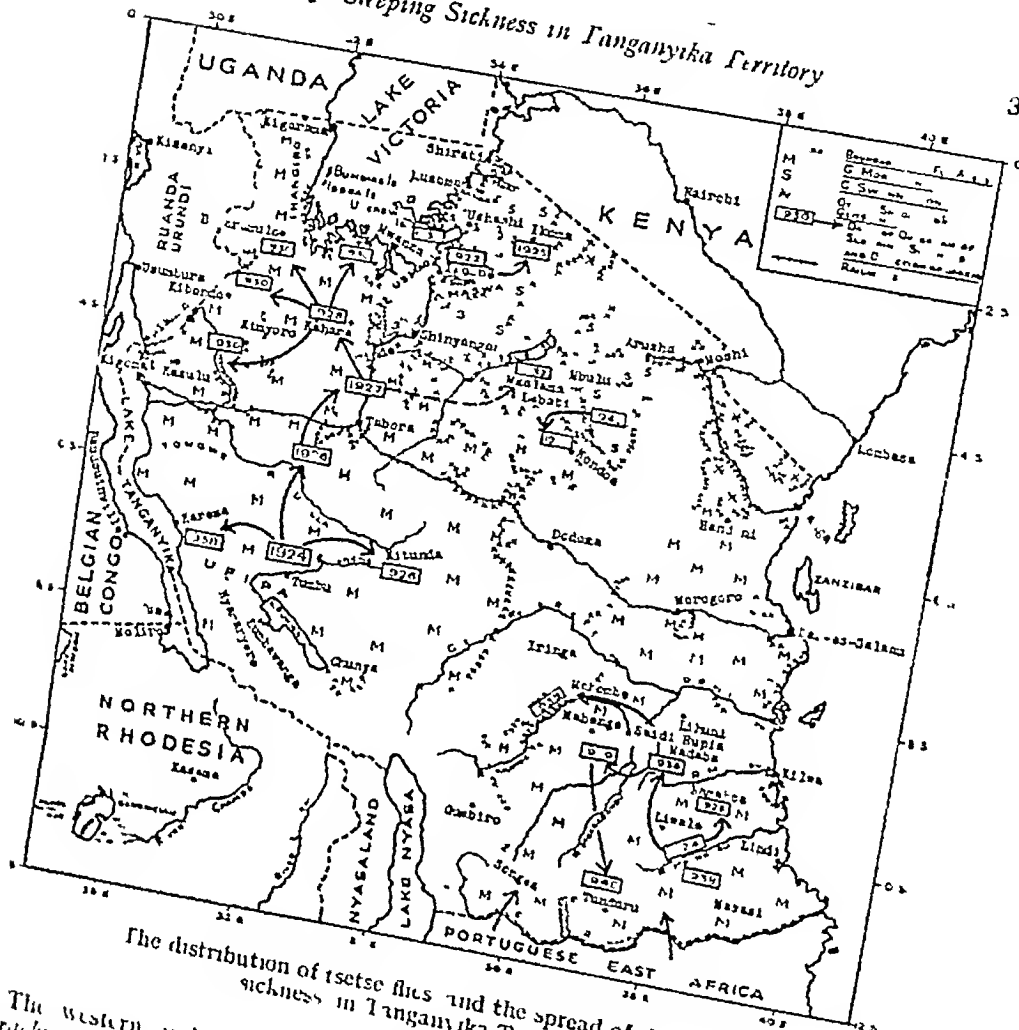
It was in the Rovuma area in 1917 that TAUTZ and HUMER (1919) inoculated themselves and 129 Africans with six different strains of *T. brucei* derived from four naturally infected horses and two naturally infected mules, without being infected: this experiment was designed to show that *T. brucei* and *T. rhodesiensis* were distinct species.

#### *The Tsetse Flies Present*

The large area of Tanganyika Territory which is infested with tsetse flies is shown on the accompanying map.

# No 1] Sleeping Sickness in Tanganyika Territory

3



The distribution of tsetse flies and the spread of sleeping sickness in Tanganyika Territory

The western and eastern fly blocks are mainly occupied by *Isobertinia* *ruficeps* (in the woodland carrying *Glossina morsitans* in which pockets of *pallidipes* and *G. brevipalpis* occur. The northern fly blocks are *Acacia* *thicket* and *G. brevipalpis* in isolated areas. In one area of Shinyanga *pallidipes* is also present in the last two areas. *G. morsitans* and *G. swynnertoni* overlap, *G. morsitans* occurs on the shores of Lake Victoria. MACLEAN (1927) *pallidipes* is at one time reached the Lake shore in many places from the Malagaris delta and that it was not uncommon to find both these species at the same spot. *G. morsitans* occurs from the Kenya border through Mbula district to the west of Lake Tanganyika. *G. morsitans* is present in the coastal belt on the east of the Territory while *G. brevipalpis* occurs just over the Kenya border.

For the detailed distribution of the various species the reader should consult POTTS (1937) or the tsetse fly map in "The Atlas of the Tanganyika Territory (1942) issued by the Tanganyika Territory Department of Lands and Mines, Survey Division.

### 3. The Recent Outbreaks of Sleeping Sickness due to *T. rhodesiense*

In 1922, sleeping sickness of the *T. rhodesiense* type was identified in Maswa District and up to the end of 1946 a total of 23,965 cases of the disease have been diagnosed microscopically in the Territory. During epidemic periods many more people probably died undiagnosed. The yearly incidence of the cases in the various areas is shown in Appendix I (p. 16) and the spread of the disease over the Territory is illustrated in the map.

**Maswa**—At the end of February 1922, a large number of African deaths were reported from the Maswa fly-block and investigations by Maclean established the fact that the cause was sleeping sickness, the responsible trypanosome being *T. rhodesiense*. The people were emphatic that the village of Igombe on the western border of the Maswa fly-block, was an early focus of the disease, and they traced its passage thence from village to village, naming each until it came to their own neighbourhood (SWYNDERTON 1923). Swynerton stated that it was always easy to trace a sequence between any case and preceding cases—going to see the sick, and taking the sick in, seem to have been the commonest sources of infection recognised by the local Africans. There was no indication of new and independent infections—every case appeared to be traceable to contact with sick persons in this province of tsetse.

**Ikoma**—There is constant foot traffic of Africans between Maswa and the hinterland tribes of Musoma District, and in the Ikoma area of Musoma District where it has become endemic, this disease was first diagnosed in the middle of 1925.

**The Western Fly-Block.**—The next outbreak of trypanosomiasis, also caused by *T. rhodesiense* occurred in the Ufipa area of the Western fly-block. The first cases were found in 1924 but MACLEAN (1927) stated that there was ample evidence to show that the disease had been there at least since 1921 and he mentions that European hunters, who visited Ufipa in 1915 reported that a disease resembling sleeping sickness was then present in the forest villages. The information was very vague and the Africans maintained throughout that the disease was new to them. MACLEAN (1926) also stated that a fatal disease established itself in the village of Tumbu in 1920 or 1921 and his account illustrated with a map, traces very clearly the spread of the disease from village to village spreading outwards from Tumbu. By 1924 the whole of the southern part of the fly block on both sides of the River Rungwa was infected.

The disease spread northwards reaching the southern and western sides of Tabora by 1926 and north of Tabora in 1927. MACLEAN (1928) observed that of 40 known cases in this area, there was not a single one who did not come within infective range of another case and he records another instance of spread from village to village. He stated that all the available evidence pointed to a man-fly spread.

Kahama was infected in 1928 and here again MACLEAN (1928a) showed how the disease spread outwards from the villages of Mitema and Msala, where the first cases seem to have occurred.

From Kahama the disease spread (1) northwards into western Mwanza, (2) north-westwards into Baharamulo district and (3) westwards into Kibondo and Kasulu districts, reaching these areas in 1930. The further spread of the

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## ERRATA

Vol. 45, No. 1 p. 96, line 2, for "40 years of age" read "4 years of age"

Vol. 45 No. 5 at the foot of p. 383 in the *Summary of Review Abstracts, Trypanosomiasis*, the following sentence "The author [VAN HOOFF] thinks that melarsen oxide is useful for the treatment of patients with resistant strains (a conclusion not shared by LOURIE)" does not correctly represent the views of Lourie, who shows, on p. 413 of the same issue, that he has confirmed van Hooft's findings. The phrase in brackets, therefore, should be deleted.

Vol. 45 No. 5, p. 388 in the abstract of the papers by SHORIT *et al.*, the reference to HUFF AND COULSTON in line 4 should read (*J Parasitology* 1947 v 33 No. 6 Sect. 2 (Supp.) 27).

Vol. 45 No. 5 p. 418 in translation of MURANO's title for Bantl read Bantl.

Vol. 45 No. 6, pp. 539-540, in the abstract of the papers by MARQUARD, the words "it was found that the lysoctithin formed by the lecithase in the blood suspensions were stabilized. It is believed that venom is the stabilizing substance" should read "it was found that blood suspensions were stabilized. It is believed that the lysoctithin formed by the lecithase in the venom is the stabilizing substance"

Vol. 45, No. 7 p. 646, the footnote to Tropical Ophthalmology article should read "For the 49th of this Series see Vol. 44 pp. 1093-1095"

Vol. 45 No. 12, p. 1100, in title to last abstract for KLAENZ, H. W read BECKHUIS, H. J

disease was limited by the fact that it had reached the Lake shore on the north, and the open, fly-free country on the boundary of the Belgian Mandated Territory in the west.

There was a steady progression of the disease through this extensive fly-block, with an interval of about two years before each new area was infected, and a further interval of about two years after infection before the disease reached epidemic proportions. Owing to the control measures undertaken, it is not known when the epidemics would have reached their peaks.

**Mkalama**—Sleeping sickness was next diagnosed in Mkalama district in 1932. MACLEAN, in an unpublished official report, gives the following history of the first case in this area. A wife had run away with another man, and the husband set out to look for her. In 17 months' travel he passed through Mwanza, Kahama, Tabora, Ufipa and down to the coast areas, and he then returned home. Within a few weeks he was ill and died, and a few months later a number of cases of sleeping sickness (*T. rhodesiense*) had been diagnosed in his village and in the valley in the immediate neighbourhood.

**Ukerewe**—A sharp, but limited, outbreak started in the Ukerewe peninsula of Lake Victoria, in October 1939 (the hottest month of the year). It is not known how the disease was introduced, but there is frequent traffic of Africans between this area and the infected areas of Maswa and Musoma.

**Babati-Kondoa**—In October, 1943 (again the hottest month of the year), cases of sleeping sickness were diagnosed amongst the African labourers working on European farms in the Babati area of the Northern Province. Most of these labourers were aliens from other districts, who had come in search of work, and at least one party of Waha had come from the western part of Kibondo district and had travelled through the Kibondo-Kahama-Mkalama infested areas before arriving at Babati.

The disease is spreading southwards into the north-western corner of Kondoa-Irangi district. There are records of African inhabitants of Kondoa travelling from Arusha through the Babati area and being diagnosed on their return home, several men, previously healthy but later infected, had been working on bush-clearing at the southern end of the Babati area.

**South-Eastern Fly Block**—In December, 1924, an outbreak of the disease occurred in Liwale district, about 50 miles north-east of the district headquarters. This small outbreak was fully described by DYE (1927). In the memory of the older inhabitants the area had a bad reputation, villages built there had sooner or later to be abandoned owing to sickness, which ceased when the inhabitants took up new sites farther away. As, however, the valleys possessed good soil and water in a dry and unprofitable area, the people usually made attempts to return, although certain sites, favourable in themselves, had become definitely banned. That sleeping sickness was well known was shown by the fact that it possessed a local name. Although Dye does not discuss how it was introduced into the area, he was certain that the disease, which had started in the village of Namabao, was spread from village to village by infected human beings. The disease eventually disappeared, apparently as a result of a further spontaneous abandonment of the whole area by the people.

In March, 1936 sleeping sickness was found at Madaba, 100 miles due north of the district headquarters, and the present author obtained the following history. Saidi Idunda, who had lived on the River Mbemkuru for about a year returned home in September, 1935, began to have fever and died in November, 1935. When he was dying, he was housed by his brother-in-law Abdullah Likurunju. A short time after Saidi's death, Abdullah fell ill and then his nephew, grand-daughter and his wife also did so. Trypanosomes being found in the blood of the last-named in April, 1936. Ali Mbiriri visited Abdullah in January, 1936 before the latter's death, and returned home with

fever and died and after his return his father fell ill and trypanosomes were found in his blood. Further patients all gave a history of having lived with or visited one of the above patients. The disease eventually spread widely in the area cases being diagnosed as far west as the River Mbarangandu, which is the boundary between Liwale and Mahenge district, and a favourite resort of fishermen of both areas.

The River Mbemkuru area was probably infected during the period of the German occupation, when sleeping sickness spread from the Rovuma to Kilwa and the disease appears to be endemic there, as cases have been found from 1924 onwards, whenever this inaccessible area has been surveyed. There is no doubt that the 1936 outbreak in Liwale was the direct consequence of the introduction of the disease from this area by an infected human being.

*Rufiji*.—Only three cases, diagnosed in 1934, 1936 and 1938, have so far been reported in Rufiji district. The last of these is particularly interesting, as the patient had lived in the village of Bagala for over a year. During September 1938, he had visited the village of Jumbe (sub-chief) Saldi Rupia in Mahenge district and he fell ill with trypanosomiasis in October on his return home. To reach Saldi Rupia's village, he would have had to travel through the northern part of the infected Liwale area.

*Mahenge*.—Isolated cases of trypanosomiasis were recognized in 1925, 1926 and 1930. The last patient was a child 2-3 years old who had visited a village on the Songea road where the local track from Liwale joins the main road.

The first case of the present outbreak, however, was diagnosed in April 1939. The patient was a Game Scout who had been stationed for some time at the village of Jumbe Saldi Rupia (see above). The next case in August was in a mission teacher at Mchombe mission. Three cases were diagnosed in September at the southern edge of the district, all of the patients gave a history of having visited Liwale district. In November, a hut counter living on the River Kilombero in the north-western corner of the district was found to be infected and in December in the same area, a relative of the teacher from Mchombe was diagnosed. The disease subsequently spread all over the southern part of the district, although in the north-west corner it remained localized.

Whether the disease was introduced to the village of Jumbe Saldi Rupia by the Rufiji traveller or whether the village was already infected by intercourse with the Liwale area, remains unknown. By analogy with the spread of the disease in the western fly-block, with the two years' lapse before successive areas were infested, one would suspect that Saldi Rupia's village was already infected in 1938 from Liwale and that it was the chief cause of the spread of the disease to Mahenge in 1939.

*Southern Province*.—Up to 1936 the cases which were recorded in the Southern Province were either in Africans from Portuguese East Africa, or else in local Africans who had visited that country.

When resettlement was taking place in Mahenge in 1940 many of the peoples of the southern part of the district moved into bush villages in Tunduru and Masasi districts, and there was a sharp rise two years later in the number of cases diagnosed in the northern parts of these districts. Some of them particularly in Masasi district may also have been infected on the River Mbemkuru.

*Lake Tanganyika*.—The first cases encountered in this area since the British Administration took over the Territory were found in 1924. Several of them occurred either in natives of the Congo or in others who had recently visited infected areas situated in Belgian territory (TANGANYIKA TERRITORY *Ann. Med. Report* 1925-23). The infection was caused by *T. gambiense*. Since then, sporadic cases were found between the Anglo-Belgian border and Tongwe,

where the disease appeared to be endemic (MACLEAN, 1927, 1930) No cases were found south of this, though a thorough search had been made since October, 1925

In 1938, cases of sleeping sickness began to be recognized at Karema, and on the southern half of the Lake. The infection of a European Telegraphic Inspector in an area south of Karema led to an extensive examination of the area, when it was found that the infection was of the *rhodensis* type. This was an extension westwards of the Ufipa outbreak, through the *morsitans* fly belts, until the disease had reached the Lake shore. A total of thirty-one officials and non-Africans have been infected since 1922. This number is made up of seven European Officers, one Sub-Assistant Surgeon and five African subordinate staff, all Government officials, and ten Missionaries, four miners, two other Europeans and two Asian traders.

#### 4 Treatment

MACLEAN and FAIRBAIRN (1932) recorded the results of treatment of 719 cases of *rhodensis* sleeping sickness, the patients were kept under prolonged observation. In Maswa district, where patients came for treatment relatively late, of 131 patients treated, twenty-one (16 per cent) were cured after an observation period of more than six and a-half years. In the Tabora (epidemic) area, where patients came for treatment relatively early, of 588 patients treated, two hundred and eighty-three (48.2 per cent) were well and probably cured, after an observation period of not less than two years and five months. FAIRBAIRN (1944) has recorded the present methods of treatment and he has emphasized that a prognosis can only be given if the cerebrospinal fluid protein has been estimated at the beginning of treatment and during an adequate follow-up period.

In any outbreak of sleeping sickness in a new area, the first patients seen are usually at advanced stages and it takes some months before the results of treatment, and of propaganda, have any effect in making patients come earlier for treatment. The cure rate of 48 per cent recorded for the Tabora epidemic is about the best one can expect in any large epidemic, and it is considered that a minimum of 11,500 of the 23,955 patients diagnosed between 1922 and 1946 have died, or will die. This is a serious loss to a country which is already underpopulated.

#### 5 Control Measures

As soon as the disease was found in an area dispensaries were built, and staffed with properly trained persons, equipped with microscopes. Treatment was soon started. Treatment alone, however, can never control or stop an epidemic, and was merely palliative until more positive preventive measures could be planned and put into operation. These control measures were based on the principle of breaking the contact between man and the tsetse fly. *Maswa*—In 1922, approximately 5,000 people were removed from the tsetse bush and resettled in the open country, but by communal bush-clearing considerable congestion in the open country, on the edge of the bush, was caused during 1926-28. The congestion was relieved and sufficient land was made available for all the people. Since 1935 only one case (in 1938) has been diagnosed in the district. *Ukerewe*—When the Ukerewe outbreak began, the Tsetse Research Department applied in the field their experimental method of 'discriminative bush clearing'. This implies the clearing of only those parts of the bush which form the essential tsetse habitat. During 1940-42, 118 square miles were treated involving the removal of 4,600 acres of hard-pan vegetation, or only 6 per cent. of the total area of bush (BAH, 1943). The tsetse was eliminated in parts or

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*Maswa*—In 1922, approximately 5,000 people were removed from the tsetse bush and resettled in the open country on the edge of the bush. This caused considerable congestion in the open country, but by communal bush-clearing during 1926-28 the congestion was relieved and sufficient land was made available for all the people. Since 1935, only one case (in 1938) has been diagnosed in the district.

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reduced in numbers in other parts, that the outbreak ceased although the people had remained dispersed in their hamlets.

*Babati*—In Babati, the method employed in 1944 was to remove the people and resettle them in open country. A measure of success was obtained, but the open country has not yet been sufficiently enlarged. Many of the cases now being diagnosed occur in people who surreptitiously return to the infested bush to collect the bananas, coffee and pawpaws which had to be left behind when they were resettled.

*Remainder of the Territory*—In the remainder of the Territory the policy adopted by MACLEAN was to make fly free settlements in the fly-bush. The aim was to have at least 750–1 000 taxpayers in each settlement the larger figure is preferable, but many of the earlier settlements had considerably less for various administrative reasons. Allowing a family of 3–5 persons per taxpayer this meant a total population of approximately 2,900–3,500 people in each settlement.

The land selected for resettlement was usually a piece of virgin *msombo* and it had to be of such size as to allow of 16 acres of good agricultural soil (excluding hills swamps, etc.) per taxpayer with adequate water supplies. As the area was a virgin one and usually heavily covered in bush, it took up to 4 years or more to clear properly the first 4 acres per taxpayer and it would take up to 12–15 years to clear the whole 16 acres per taxpayer with all the work being done by an annual turn-out of communal labour. The incidence of the disease was only affected therefore, about 2–4 years after the people had been resettled. FAIRBAIRN (1943) has given a full account of the details in making these resettlements. Table 1 shows the number of settlements made in each area.

TABLE 1

*The number of settlements made and the number of people moved each area.*

Area	No. of Settlements	Year resettled	Taxpayers moved	Family per Taxpayer	Total people moved approximately
Matua	to open country	1923			8,000
Uda	10	1925/27	minimum of 8,540	3.3	28,500
Tabora		1928/37		3.3	4,300
Kahama		1928/29		3.3	44,700
Kibondo	4	1933	13,848	3.3	13,800
Kamala					
Baharawulo	6	1933/34	4,113	3.5	8,400
W. M. area	9	1934/36	6,497	4.0	26,000
Mabenge	1	1941/45	450	—	1,372
Babati	1	1944	2,000	—	8,000
Lwale	1	1945			
Total	48		28,656		138,872

Approximately 140,000 people have been removed from isolated bush hamlets and resettled, either in settlements or in open country. By referring to Appendix I, it will be seen that such resettlement had a marked influence on the number of cases of sleeping sickness diagnosed in subsequent years.

Maclean has often been severely criticized for making settlements in the fly-bush, particularly as many of them were 150 miles or more from the railway and administrative headquarters and the roads to them are often closed for 6 months or more during the rains. But there are a number of points which the critics have overlooked.



Sleeping sickness occurs in a population which is widely dispersed in isolated hamlets in the fly-bush. It is considered that the condition most favourable to an epidemic is a density of population of 5 to 25 taxpayers (*viz* 16 to 80 people) per square mile. With a density of less than 10 people per square mile the disease can occur, but the population is usually so scattered that the infection is self-limited while with a density of 100 people or more per square mile, many of the villages are large enough to protect themselves from tsetse by the clearings made for their farms.

By the very nature of things, the people who elect to live in such widely scattered conditions are the most primitive in the Territory. They are the hunters who do little agriculture, or else the malcontents and the very conservative who desire to escape from tribal authority and from the restrictions and controls of progressive administration. MACLEAN (1929b) has ably summarized the position, and his paper should be consulted. Despite their primitive outlook, these very same people have an intense attachment to their tribal lands, and refuse to be moved out of their tribal area. They had, therefore, to be settled on their own land. It was difficult enough for the administrative officers to organize the present settlements, it would have been impossible to make settlements by moving the people right out of their tribal area.

Where a Native Authority had enough people to make one or more settlements of the correct size, these could be sited anywhere within the tribal lands. But where the people concerned were too few to make a settlement on their own, they were usually moved to the boundary of their area and joined up with a settlement of the neighbouring Authority, to make one large area with the tribal boundary running through the settlement.

Even at present there is some tendency to re-establish bush hamlets, and one of the main reasons for this is the fact that the head of a family moves out to settle on the boundary of the tribal area and often at his suggestion.

When the Ufipa settlements were made in 1925-26 they were in Ufipa district (Sumbawanga) in the south-west of the Territory, and the settlements were before placed as far south as possible, in order to reduce the distances to be travelled with porters, on inspection and for the disposal of produce. Some years later the district boundaries were re-aligned, and the Ufipa settlements came under the administration at Tabora in the centre of the Territory and on the railway line. If Tabora had been the administrative headquarters in 1925, the settlements could have been sited at least 50 miles further north and nearer to the railway line, but it was now too late. The same remarks apply to settlements which are now in Chunya district but which were formerly under administrative charge from Tabora.

Finally, even if the people could have been moved out of the whole of the south-western fly-block and settled on or near the railway line, it would have involved leaving a vast area of country completely uninhabited and unadministrated, which was politically undesirable.

In two areas the disease appears to have been completely eradicated—in Maswa by settling the people in open country and in Ukerewe by eliminating the fly by discriminative bush clearing. The soundest control measure would appear to be a combination of the two methods, *viz*, settling the people in open country which has been enlarged to receive them and then discriminative clearing of the bush over a fringe half a mile wide, so that the people visiting the immediate forest for firewood, building poles, grass, etc., would not come in contact with tsetse.

## 6. The Sex Incidence of the Disease

The sex of the patients infected is shown in Table 2, the figures referring to cases diagnosed from 1936 onwards.

TABLE 2

*The Sex of Persons suffering from Sleeping Sickness in the various Areas.*

Area	Males	Females	Boys (3-15 yrs)	Girls (5-15 yrs)	Infants male	Infants female	Totals
Ufipa	732	88	22	9	1 (3 yrs)	—	863
Tabora	221	34	9	2	—	—	266
Kahama	878	186	89	18	1 (3 yrs)	—	1,169
Western Mwanza	67	10	4	2	—	—	83
Kibondo	842	142	36	17	1 (2 yrs)	2 (3 yrs)	1,040
Kasulu	217	42	6	—	—	—	266
Biharamulo	156	30	2	3	—	—	193
Ikoma (Mwanza)	301	128	21	14	—	—	462
Ukerewe	172	94	21	10	7 (1-4 yrs)	1 (4 yrs)	321
Mkalama	53	31	7	3	—	1 (3 yrs)	97
Bubati	308	70	10	8	1 (1½ yrs)	1 (3 yrs)	423
Kondoa	62	47	8	2	1 (3 yrs)	—	137
Litale	63	55	7	7	1 (2 yrs)	1 (3 months)	136
Mahenge	116	64	16	6	2 (2 yrs, 4 yrs)	2 (10 months, 4 yrs)	204
Rovana (Southern Province)	129	102	13	12	1 (3 yrs)	2 (3 months, 3 yrs)	259
L. Tanganyika shore	32	12	1	—	—	—	45
	4,441	1,104	238	118	16	10	5,907

In the old settlements of Ufipa, Tabora, Kahama, Western Mwanza, Kibondo, Kasulu and Biharamulo which were made between 1925 and 1936, there was a marked preponderance of males, the proportion of adult men varying from 79.2 to 85.0 per cent. with only 5 children aged 2-3 years infected in a total of 3,820 cases (0.13 per cent.) In these areas, it is the men who leave the settlements to hunt to collect beets and to transport produce and they are often accompanied by boys of 12-15 years of age.

On the other hand in the areas of Ikoma, Ukerewe, Mkalama, Kondoa, Lindi, Mahenge and Southern Province where epidemic conditions prevailed for a greater part of the period under consideration, the proportion of women was high varying from 27.3 to 40.4 per cent. with 21 infants and children aged from 3 months to 4 years infected in a total of 1,617 cases (1.3 per cent.) The fly was, therefore, present in the huts and in the immediate surroundings, where the women were at work.

Three infants, 3, 8 and 10 months old, were infected, as well as quite a number of other small children, and the incidence in infants and children would have been greater had the records of the Kahama epidemic of 1928-29 and of the Kibondo epidemic of 1933-34 been available. There was no evidence in our experience that infants had any inherited immunity. Whether they were infected or not depended upon the closeness with which they were brought into contact with the fly.

DURK (1923) in his report on the Maswa epidemic stated that the majority of the cases seen were in adults, both men and women and that the disease was rare in young people below the age of fifteen and exceedingly rare in young children. He stated that the age distribution thus corresponded to what

observers in the Congo had learnt to associate with human trypanosomiasis in epidemic, as opposed to endemic, form. In Tanganyika Territory, however it is characteristic of epidemics that a high proportion of women, children and infants are infected.

### 7 Variation in the Incidence of the Disease

#### A Monthly Variation

The effect of temperature on the transmissibility of the polymorphic trypanosomes by *Glossina* has long been known. KINGHORN, YORKE and LLOYD (1913) showed that the earlier stages of the development of the trypanosome in the fly could occur at a comparatively low temperature ( $60^{\circ}\text{F}$ ,  $15.6^{\circ}\text{C}$ ), that the trypanosomes could persist in this stage for at least sixty days without the salivary glands being invaded, but that for the completion of the cycle it was necessary for the temperature to which the flies were subjected to be raised to a considerable extent ( $75^{\circ}\text{--}85^{\circ}\text{F}$ ,  $23.9^{\circ}\text{--}29.4^{\circ}\text{C}$ ). They also found that the percentage of infected "wild" flies caught in the Luangwa Valley was greater in the hot than in the cold season, and an examination of their Table 13 shows that the highest percentages were found when the mean external shade temperature was  $79.0^{\circ}\text{--}87.1^{\circ}\text{F}$  ( $26.1^{\circ}\text{--}30.6^{\circ}\text{C}$ ) while between  $67.2^{\circ}$  and  $77.5^{\circ}\text{F}$  ( $19.6^{\circ}\text{--}25.3^{\circ}\text{C}$ ) no infected flies were found. LLOYD (1930) and TAYLOR (1932) had shown that it was possible in the laboratory to obtain greatly increased infection rates by incubating the tsetse flies at  $33^{\circ}\text{--}37^{\circ}\text{C}$ . A more recent finding by BURTT (1946) was that when pupae of *G. morsitans* were incubated at  $30^{\circ}\text{C}$  the flies that emerged gave much greater transmissibility rates than flies which had come from pupae kept at normal (and lower) laboratory temperatures.

At Tinde Laboratory it has been found that the percentage of flies infected in each month is correlated significantly with the mean maximum temperature to which the flies are exposed. The highest transmissibility rate is obtained in October at the height of the hot, dry season, and the lowest in May-July, in the cool period after the rains.

Table 3 shows the number of cases of sleeping sickness diagnosed in each month totalled over a period of years and the average monthly mean maximum temperature recorded at the Meteorological Station Tabora, for the period 1936-46. Tabora is situated in the centre of the western fly-block, at an altitude of 4 000 feet, and the temperatures recorded there are representative of the whole of the area.

In the western fly-block as a whole there was a very significant correlation between the monthly mean maximum temperature at Tabora and the number of cases of sleeping sickness diagnosed in the following month ( $P < 0.1$ ), and this level of significance was maintained when the figures for individual areas were examined, with the single exception of Ufipa. In the Kibondo-Kasulu-Biharamulo areas, taken together there was also a very significant correlation ( $P < 0.1$ ) between the maximum temperature and the number of cases diagnosed two months later. This correlation is shown diagrammatically in Fig. 1.

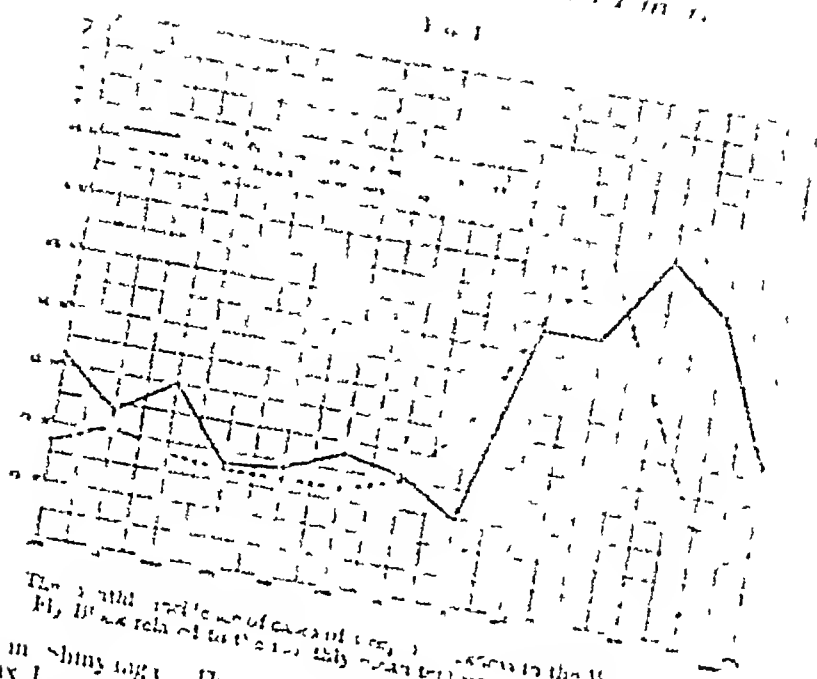
No suitable temperature data were available for comparison with the cases in the remainder of the Territory. The increase in the number of cases noted in the hot dry season is thus probably due to the combined effects of occupation, leading men into the fly bush and an increased proportion of infected flies encountered, owing to the high temperatures of that period.

#### B Yearly Variation

The Tsetse Research Department take as their index of the fly population in the bush the number of old male *G. swynnertoni* caught per 10,000 yards on fly

TABLE 2.  
The monthly incidence of cases of Sleeping Sickness

	Jan.	Feb.	March	April	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.	Total
Ulupa	114	118	136	104	93	91	104	75	63	113	130	176	1,317
T. born-Ninga	134	162	169	112	102	153	137	112	181	210	310	310	1,824
Kohama	328	336	329	323	317	309	323	300	332	487	504	423	4,697
W. Mwanza	31	16	23	16	15	16	13	15	15	11	19	1	190
Kulobondo	406	308	320	265	297	340	331	353	378	360	456	493	4,214
Kamal	33	53	48	37	31	41	43	24	41	84	53	47	531
Debarausalo	30	30	35	19	28	33	27	45	16	21	24	36	316
Average mean maxi- mum temperature (°C.) Tabora, 1934-48	37.7	26.1	27.6	27.7	27.7	27.7	28.0	29.1	31.1	32.3	30.1	28.0	
Mara	28	16	24	23	14	15	15	6	20	10	19	35	231
Ikoma	55	80	77	60	76	58	52	86	74	77	81	51	877
Ukarere	23	31	19	21	25	23	26	16	14	43	40	43	323
Mkalania	6	6	—	4	6	6	11	9	3	13	14	37	107
Ikabati	34	47	63	37	33	36	31	40	44	45	43	29	485
Koodon	—	—	1	3	—	3	13	23	23	16	26	16	144
Iberville	30	37	41	44	44	34	33	23	18	30	19	13	378
Mabanga	19	10	15	19	33	36	35	30	30	30	13	13	366
S. Uvuhaca	13	34	24	30	33	19	34	33	25	15	18	17	373
L. Tanganyika shore	6	4	10	6	4	3	13	6	10	10	8	12	89
Total	1,376	1,343	1,331	1,144	1,178	1,195	1,206	1,137	1,048	1,546	1,776	1,636	16,219

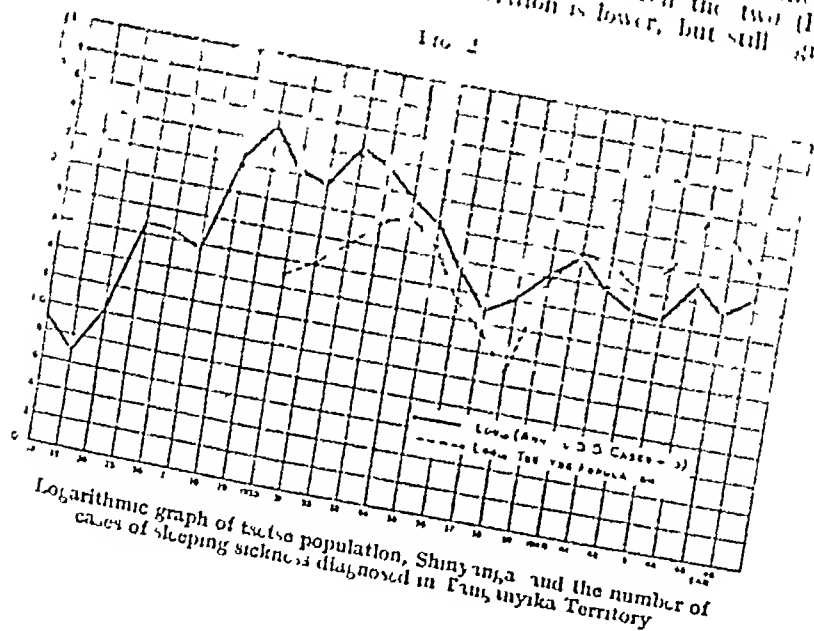
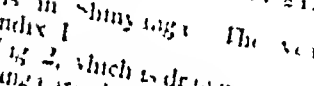


The annual catch of each of these species in the Western Fly, by a catch of 100 fish, only about 100 fish are at Filson's Shiny log. The yearly average of these catches is given in 1, which is drawn on a logarithmic scale, the catch is shown in units the number of fish caught in the territory. State

rounds in Shimmytagi. The yearly average of these catches is given in Appendix I.

In Fig. 2, which is drawn on a logarithmic scale, the catches of test cells in Shimmytagi are shown against the number of cases of sleeping sickness diagnosed in the whole territory. Statistical analysis shows that over the period 1930-45 there is a very significant correlation between the two ( $P < 0.01$ ). When the year 1946 is included the correlation is lower, but still significant.

Fig. 2



(P nearly equals 0.7) The outbreak in Koodoe Irangi may be responsible for the adverse effect of the 1946 figures on the total correlation. There is a suggestion of a cyclical variation, but the observations are too few.

A study of Appendix I shows that sleeping sickness has usually reached epidemic proportions in new areas in the same years that maximum numbers of cases have occurred in distant endemic centres (which might have a different species of fly) e.g. compare in 1932 Ikona-Ufipa-Tabora with Kibondo in 1940 Kibondo with Ukerewe-Mahenge and in 1944 Kahama-Kibondo with Babati. Further in the years 1927-1937-38 and 1942-43 minimal numbers of cases occurred in widely separated areas. The yearly variation in the tsetse population is probably due to a long-term variation in climatic conditions. One of the climatic factors may be temperature, but there are probably other unknown factors at work over a long period. The variation in the number of cases of sleeping sickness may be directly correlated with the tsetse population (i.e. the more flies there are the greater the chance there is of being bitten and hence of more cases). On the other hand, the correlation may be indirect, through climatic conditions influencing both the tsetse population and the infection rate of the fly.

### 8. The Role of Game

In the foregoing study of sleeping sickness in Tanganyika Territory it has been shown that the introduction of the disease into an area can usually be traced to the arrival of a human being infected with *T. rhodesiensis*. There is no need to postulate the repeated infection of man with *T. brucei* derived from game. It has been shown, however, that a strain of *T. rhodesiensis* passed through sheep and antelope by cyclically infected *G. morsitans* was still infective for man ten and a half years after its removal from man (FAIRBANKS and BURTT 1946). The rôle of game is that when once the disease has been introduced into an area the game become infected with *T. rhodesiensis* and they then act as reservoirs for maintaining the disease endemically.

The statement that game act as reservoirs for *T. rhodesiensis* has been criticized on the grounds that this has only been demonstrated hitherto in the laboratory, and that *T. rhodesiensis* has never been recovered from game in its natural state but this criticism has been answered.

MACKECHAM (1944) reported an epidemic of Rhodesian sleeping sickness which began in November 1940 and swept through the Busoga and Samia districts of Uganda. In April 1943 Dr C. H. N. Jackson of the Tsetse Research Department, was working on the insect vector of this epidemic, and he was engaged in collecting tsetse flies in the Lugalla area of the Samia district. The area where the flies were caught had been cleared of all inhabitants at least year before the nearest human source of trypanosomes was about 3 miles distant from where the flies were found and the only persons entering the area were very occasional trespassers in search of fish and game. While collecting the flies one of Jackson's fly-boys from Tanganyika Territory became infected with sleeping sickness.

The flies caught were fed in batches of 100 on each of fifty clean laboratory bred rats, and it was estimated that 3,500 flies fed. When feeding was completed, the flies were killed and examined. One *G. palpalis* was found, and the rat on which this fly had fed was discarded all the rest of the flies were *G. palpalis*. Five rats were infected with polymorphic trypanosomes with incubation periods of 7 days in each case. The five rats were killed, 0.25 cc. of heart blood was mixed with 0.25 cc. of sterile normal saline and injected into the arm of each of five volunteers. Four of the men showed no reaction and their blood was negative up to the 10th day after inoculation when they were given treatment. On the 4th day the fifth man developed a painful swelling

at the site of the injection, on the 5th and 6th days his temperature was 102°F, and on the afternoon of the 6th day scanty trypanosomes were found in his peripheral blood. He was then given treatment. The volunteer was an employee of the Medical Department and lived at Junja, where he was out of contact with the fly.

This experiment establishes the fact quite clearly that *G. pallidipes* was carrying a polymorphic trypanosome, infective to man and morphologically identical with *T. rhodesiense*. The area was as completely depopulated as anyone is ever likely to find for the purposes of such an experiment, and there is no doubt that the fly could have been infected only by feeding on an animal reservoir of the trypanosome.

Epidemiological evidence that game act as reservoirs for the human disease also comes from two areas in Tanganyika Territory. The River Ugalla, in the Tabora district, was depopulated in 1925-26 and except for an occasional foot-traveller, there are no human beings in the area during the six months of the wet season. Fifty miles to the east of Kibondo are the native-worked salt deposits of Kinyora which are only visited (illegally) for 2-3 months at the end of the dry season. In both of these areas cases of sleeping sickness occur as soon as the fishermen return to fish the Ugalla pools in June, or the people of Kibondo district go to the salt deposits in August.

Dr C H N Jackson, in a personal communication states that in the field, the average length of life of male *G. morsitans* varies from about 2 weeks in the hottest time of the year up to 5 or 6 weeks during the rains. The extreme span of life is believed to be about 12 weeks. The female flies live for an average of perhaps 2 months. It is not possible for a fly which has been infected from a human being in November of one year to be able to infect a human being in June of the following year. The infected flies which are present in June of any year can only have obtained their infection from any existing game which were acting as reservoirs of the parasite.

It is therefore, understandable why the disease has not died out in Tanganyika Territory although resettlement has controlled its incidence. So long as it is necessary to make settlements in fly-bush containing an abundance of game, visits to or through the bush will be dangerous and so long as game are present and act as reservoirs of the parasite, the disease can only be reduced in incidence, not eliminated.

**Acknowledgments**—I have to thank my colleague Dr K C Willett, for the large number of statistical analyses which he made, and for drawing the figures and map. Dr C H N Jackson of the Tsetse Research Department, for his help and criticism in the statistical work. Mr W H Potts of the Tsetse Research Department for providing the figures of the tsetse population and for giving his permission to publish them and the Hon the Director of Medical Services Tanganyika Territory for his permission to publish this paper.

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## SUMMARY OF RECENT ABSTRACTS \*

### I CHOLERA

#### Epidemiology Aetiology

STOWMAN (p 208) has written an account of the world cholera situation in the summer of 1946, in China at least 16 provinces were affected, and Thailand and parts of India had a bad year. The same author (p 421) makes the point that the 1946 epidemic of cholera in China was one of the most extensive ever recorded in the Far East. He thinks that there are two completely distinct main foci, in the Yangtze and Kwangtung areas respectively. The type of disease seen in the former is more amenable to treatment than that seen in Kwangtung.

PETERSON (p 1065) shows that the risk of infection in an outbreak in China was about 36 times as great in household contacts as in the general population, and about 5 times as great in unvaccinated as in vaccinated contacts. The information on which these figures are calculated is admittedly so likely to be erroneous that he claims only that the figures are rough indications.

He (p 1065) found in China that the average period required for stools to become negative for *V cholerae* was  $5.4 \pm 2.3$  days from the onset of symptoms. In no case were stools positive beyond the 17th day.

PANJA and GHOSH (p 998) found true *V cholerae* in 16 of 524 samples of water from the river Hooghly. They used the candle-boric-peptone-water method.

\* The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin* 1947 v 44. References to the abstracts are given under the names of the authors quoted and the pages on which abstracts are printed.

GALLUT (p. 421) contends that the true cholera vibrio is not Voges-Proskauer negative, as it is usually held to be, but that it can produce acetylmethylcarbimol in sensitive media. It produces considerably less, however than the El Tor and the Celebes vibrios, and this fact can be used (as well as the haemolysis test) as a basis for differentiation. In a highly technical paper the same author (p. 660) discusses the oxidation-reduction potential of the cholera vibrio under various conditions of cultivation. The original paper should be consulted for details.

SKID and his colleagues (p. 206) discuss in two articles, the biochemistry of the cholera-red reaction—these papers cannot satisfactorily be summarized, and should be read in the original.

BRUMMAN (p. 660) has isolated a non-agglutinable vibrio from a patient with typical (but not fatal) cholera in Tonking.

### Pathology Treatment

CHATTERJEE (p. 906) has continued his studies of the bone marrow in fatal cases of cholera, and shows that the characteristic finding is the very great dilatation of the capillaries and sinusoids, which was most remarkable in the bone marrow but which was also found in many organs. This dilatation, it is suggested, may partially explain the collapse which is a feature of cholera.

In the report of the Scientific Advisory Board of the Indian Research Fund Association for 1946 (p. 906) there is a statement of the results of trials of treatment with various sulphonamides. There is little to choose between the results with sulphaguanidine, sulphasuxidine, sulphadiazine and controls given a placebo so far as case-mortality is concerned. CHU HUANG and their colleagues (p. 423) have used sulphaguanidine and sulphadiazine in the treatment of a small number of patients with cholera, in addition to intravenous saline. The results indicate that the average duration of diarrhoea was reduced, but there was no remarkable effect on the time of disappearance of vibrios from the stools. The effects of the two sulphonamides were about equal.

REIMANN *et al.* (p. 423) in China treated a few patients with streptomycin but do not report any striking favourable results. They think that the important clinical feature of cholera is not intoxication but dehydration and that correction of the latter is the chief therapeutic need. If treated properly in this way cholera becomes much less fatal, with a case-mortality rate of only 5 per cent. Streptomycin and the sulphonamides showed no significant effect in reducing the duration of the carrier state in convalescence. The authors think that cholera is not only water-borne, but is also transmitted directly from case to case—the latter mode of spread was more important than the former in the outbreaks they describe.

PETERSON (p. 1085) has attempted to evaluate the value of sulphadiazine prophylaxis of cholera in China, but the number of cases which occurred in the trial and control groups was so small that no final conclusions were possible.

### Vaccination Control

BURROWS *et al.* (p. 422) in their introduction to a study of immunity to cholera, comment on the fact that there is little positive evidence on the subject of the efficacy of vaccines—but they conclude that the immunity produced may be in some small degree effective, though leaving much to be desired. The cholera vibrio in its infection remains within the lumen of the gut, that is, virtually outside the tissues of the body throughout the disease. The same authors (p. 422) have investigated the structure of the O antigen of the cholera vibrio and describe three effective components, A B and C. A is group-specific B and C are type-specific for Inaba and Ogawa strains. The possible

are, therefore, A, AB, AC and ABC, the last is the Hikojima inter-ate type. The authors propose nomenclature according to these letters, and of the old names, they note that the O group I of Gardner and Ven-uman contains group-specific antigen A, and that there is no immunological action between cholera vibrios and El Tor vibrios of O group I.

The Report of the Scientific Advisory Board of the Indian Research Fund 946 (p 998) it is stated that of 320 strains of *V. cholerae* isolated, 88.1 per cent were of Ogawa type, and 11.9 per cent Inaba.

UNJA and DAS (p 999) have made a preliminary study of the intradermal inoculation of cholera vaccine in man, and report encouraging results. BODWARD (p 79) reports that a number of men in the U.S. Navy developed symptoms suggesting appendicitis after, and apparently owing to, injection of cholera vaccine.

SEAL (p 208) notes that in part of Bengal there were 27 outbreaks of cholera in one year. He describes the detailed instructions given to patients and attendants, in relation to treatment (with sulphaguanidine) and prevention. Aching powder solution is used for domestic sterilization of discharges, and the hands, water and milk should be boiled and food should not be eaten.

Details should be sought in the original.

Charles W. Wilcocks

## RABIES

ERARAGHAVAN, N. Cultivation of Rabies Virus *in vitro* [Correspondence] *Nature* 1947, June 7, 782.

The author has previously reported [this *Bulletin*, 1947, v 44, 635] that the rabies virus will grow in a cell-free medium containing steamed sheep-brain extract, sheep serum, glycine and peptone. The addition of tryptophane (2 mgm per cc) stimulated the growth to 25 million MLD in place of 10 million MLD per cc. The addition of biotin, thiamin hydrochloride, pyridoxine hydrochloride, calcium pantothenate, nicotinic acid and riboflavin gave concentrations of 100 million to 50 million MLD per cc. By adding all these substances it was possible to dispense with the sheep-brain extract in the medium. With a medium containing 2.5 per cent glycine, 2 per cent sheep serum, 0.15 per cent peptone, 2 mgm per cent tryptophane, 2 µgm per cc each thiamin hydrochloride, pyridoxine hydrochloride, calcium pantothenate, nicotinic acid and riboflavin, together with 0.2 cc per 100 cc of biotin solution, concentrations of 5,000 million MLD per cc were obtained. The virus was also cultivated in a cell-free medium containing 5 per cent glycine, 0.3 per cent peptone and 4 per cent sheep serum. The successful cultivation of the biological agent of rabies in the cell-free medium indicated that it is not a virus in the ordinary meaning of the term. [See also this *Bulletin*, 1946, v 43, 194; 1947, v 44, 634.]

C. M. Wenyon

UBRY, G., LAFFARGUE, P. & PORTIER, A. Deux cas d'accidents nerveux de la vaccination antirabique [Two Cases of Neuroparalytic Accident after Anti-Rabies Vaccination.] *Algérie Méd* 1947, Feb, No 2, 169-72, 173-4, 175.

The author describes two cases of neuroparalytic accident occurring after anti-rabies inoculation, it was possible to show that one of these was first caused by the rabies virus. The method employed was the classical one of giving daily inoculations of suspensions of rabbit cords of increasing virulence. The

NASCIMBENE A. & PREZIOSO A. La lotta antimalarica in provincia di Pavia (studio riassuntivo degli anni 1932-1945) [Antimalaria Campaign in the Province of Pavia.] *Riv Ital d'Igiene*. 1947 May-June, v 7 No. 3/6, 192-212 1 map & 2 charts. English summary (6 lines)

This is a description of the Province of Pavia, from a malaria standpoint, and of the activities of the Provincial Antimalaria Committee. There has been very little endemic malaria in recent years. In 1932, there were 144 notified cases in 31 communes in 1945 there were but 4 cases in 3 communes. In addition, there were numerous imported cases at the time of the Abyssinian war and during the world war. Very little has been done in the matter of anopheline control. Nearly all infections are due to *P. vivax*.

Norman White

MATHIEU M. Le paludisme dans l'Atacora. Circonscription médicale de Natitingou Dahomey (Malaria in Atacora District (Dahomey)) *Bull Mèd de l'Afrique Occidentale F a para*. 1948, v 3 No. 2, 267-9

Three different tribes occupy the Atacora Circle which occupies an area of 22,000 square kilometres and possesses a total population of 148,000. The author was struck by the infrequency of mosquitoes there and, therefore, examined the degree of malarial endemicity in the region.

Figures of attendances at medical institutions from 1938 to 1945 indicated that the number of cases of malaria notified varied between 3 and 8 per cent. of all patients seen (from 9,214 persons examined in 1936 to 21,090 in 1945).

These figures are however only applicable to urban centres the author therefore consulted the records of the local sector of the Mobile Hygiene Service, which indicated that the percentages of blood films found positive for malaria for 1943 to 1945 were respectively 50.12 (28,648 blood examinations), 51.87 (28,288) and 73.90 (55,046) the most recent parasit rate was therefore about 74 per cent.

Clinical malaria in children was frequent and serious and was caused entirely by *P. falciparum*. Splenic indices from children aged 2 to 12 years in three schools are given as 23.78, 14.31 and 11.17 per cent. [but it is noted that only 185, 35 and 170 children were examined].

The gametocyte rate varied between 12 and 14 per cent. The author fixed the Ross index at 50 [it is not stated whether the endemic index of Ross or the index of Ross of Brumpt is implied].

The author concludes that Atacora should be considered as an area of high endemicity and points to the danger inherent in the casual attitude of the inhabitants to malaria because of the comparative rarity of mosquitoes [the mosquito vectors are not mentioned].

H. J. O'D. Burke-Gaffney

HAIRSTON N. G. BANG F. B. & MAIER, J. Malaria in the Natives of New Guinea. *Trans Roy Soc Trop Med & Hyg*. 1947 July v 40 No. 6, 795-807 5 figs. & 1 map.

An examination of spleens and blood smears was carried out in nine different areas of New Guinea the results are tabulated. Over 4,000 natives were examined. Malaria was found to be hyperendemic in all areas but there was considerable variation in the intensity of transmission. In one village malaria was so intense that the incidence of palpable spleen was highest in the 0-5 age group older children had sufficient immunity to determine a lower spleen rate. The spleen rate of children in this village was 68 per cent. but it had

## Malaria

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more malaria than had another village with a children's spleen rate of 94 per cent. These observations indicate the importance of classifying results according to age groups.

The authors consider the plasmodiometric index, measuring the parasite load of the population [see this *Bulletin*, 1943, v 40, 739] to be a useful adjunct to the standard survey, the positive blood smears are divided into categories according to the number of parasites found per 500 white blood corpuscles.

Norman White

PAUL, J. H. & BELLERIVE, A. A Malaria Reconnaissance of the Republic of Haiti. *J. National Malaria Soc.* 1947, Mar., v 6, No 1, 41-67, 4 figs [13 refs]

The Republic of Haiti occupies the western third of the second largest island of the West Indies, the remaining two-thirds constitute the Dominican Republic. The Gulf of Gonave almost bisects Haiti into two peninsulas. The country is mountainous. There is only one river of any size, the Artibonite. Most of the other streams are intermittent, nearly all are blocked at the mouth by sand or gravel bars, the resulting lagoons are productive of anophelines. The principal human settlements are on the coast near such streams. The population of the Republic is almost entirely Negro. The few whites and Asiatics are confined to the more important commercial centres. The economy of Haiti is about two millions. Port-au-Prince, the capital, has between 100,000 and 200,000 inhabitants, there are no other large cities. The economy of Haiti is purely agricultural. No reliable vital statistics are available.

In 1940, arrangements were made between the National Health Service and the Rockefeller Foundation to carry out a malaria survey of the whole republic. The field work was limited to an examination of schoolchildren. All schoolchildren were examined for splenomegaly. The blood of all children with enlarged spleens and of 25 per cent of children with normal spleens was examined. In villages with less than 50 schoolchildren all were examined for parasites. In all 31,285 children in 826 primary schools were examined. The spleen rate of children in schools at altitudes of less than 1,000 feet was 29.8, between 1,000 and 2,000 feet 13.5, over 2,000 feet 6.2 per cent. The highest spleen rate (20.6) and the largest average spleen of an area, the higher was the age group, 0-4. The higher the splenic index of an area, the higher was the incidence of parasitaemia both in those with normal spleens and in those with splenomegaly. For the country as a whole, children with normal spleens had a parasite rate of 21 per cent, the group with the smallest amount of splenic enlargement, palpable on deep inspiration, had a parasite rate of 68, parasite rates of 78, 80, 80 and 100 per cent were found in children with ascending sizes of spleen. Of all infections, 86.6 per cent were *P. falciparum*, 8.9 per cent *P. malariae* and only 1.9 per cent *P. vivax*. Only 2.6 per cent were mixed infections, slides were not ordinarily studied for more than five minutes.

Three species of anophelines were found. *A. albimanus*, *A. grabhami* and *A. vestitipennis*. *A. albimanus* was ubiquitous. It had a wide variety of breeding places, but preferred a sunlit situation. *A. vestitipennis* was found breeding only in one shaded swamp. *A. grabhami* was found in 19 of the 27 arrondissements breeding with *A. albimanus* or alone in streams or canals that were heavily shaded. Numerous dangerous breeding areas are man-made.

The clinical manifestations of malaria rarely arrest attention except among the infants of the community. The few areas of Haiti that are malaria-free are the higher mountain valleys and the south-west slopes where the rainfall is very low.

Norman White

NIXTO CAICEDO M. Epidemia regional de malaria en la cuenca del Lago de Maracaibo 1942-1943 [A Regional Epidemic of Malaria in the Basin of Lake Maracaibo, Venezuela, in 1942-1943.] XII Conferencia Sanitaria Panamericana. Cuadernos Americanos. Publicaciones de la Comisión Organizadora. No. 22. Caracas. 1946, June, 288+xx pp., 32 figs. on 1 pl., 8 maps (8 folding) & 43 graphs (10 folding) [23 refs.] English summary

This study of close on 300 pages, discusses in very considerable detail, and with a wealth of tables, charts, diagrams and other illustrations, a wide regional epidemic of malaria which occurred in Venezuela in 1942-43 and the measures applied against it.

The area concerned was the basin of the Maracaibo Lake in Zulia State.

Topographical and meteorological data are fully discussed: the level of the lake is inconstant and flooding into surrounding country leads to the formation of breeding places for mosquitoes. The local temperature averages about 82°F the humidity ranges from 70 to 85 per cent., and the rainfall varies greatly: an unusually heavy rainfall during 1942 preceded and contributed to the epidemic.

Sociological features are described and the incidence of malarial morbidity and mortality is discussed at length. The local distribution of anophelines is shown and it is noted that *A. albimanus* is more prevalent in the northern desert-like regions and *A. darlingi* in the southern jungle. It is stated that previous epidemics of malaria have shown some "para-quinquennial periodicity".

Full figures are given for the prevalence of anophelines in breeding places and dwelling houses in the city of Maracaibo: the obcyt rate was 5 per cent. The epidemic lasted from November until March, with a peak in January: during that period, 17,201 cases were actually recorded but it was estimated finally that the total was in the neighbourhood of 40,000.

In 7,960 blood films examined, an infection rate of 50.4 per cent. was found. In the town of Maracaibo, *P. oswaldi* prevailed, but *P. falciparum* was prevalent in 40 per cent. of the rural outbreaks seen.

The general mortality for Zulia State as a whole surpassed in 408 deaths the expected mortality according to the median: and the mortality from both malaria and fever together exceeded by 473 the corresponding median.

The control measures adopted included free distribution of 50,000 complete quinine treatments and the usual methods of controlling *Anopheles* larvae and adults.

[This study represents a very fully documented account of an extremely large epidemic.]

H. J. O'D. Burke-Gaffney

ANGELINI, G. Incertezza dei reperti di forme exoeritrocitarie del plasmodi della malaria umana nel midollo osseo [Unreliability of Reports of Exoerythrocytic Forms of Parasites of Human Malaria in the Bone Marrow.] *Riv. di Parasitol.* Rome. 1947 Mar v 8 No. 1 3-18 [Refs. in foot notes.] English summary (7 lines)

The author examines the various records which have been made of the occurrence in smears of the bone marrow and other organs and in sections of tissues exoerythrocytic schizonts of human malarial parasites. He finds that ached portions of the cytoplasm of cells may simulate these stages, as occurs commonly in smears of bone marrow and comes to the conclusion that up to the present no reliable morphological record of these stages in human malaria has been made. The paper is a useful one in that it reviews the various papers which have been published on this subject.

C. M. Haydon

Vol 45 No 1] **BLACK, R H** *The Consumption of Haemoglobin by Malaria Parasites* *Ann Trop Med & Parasit* 1947, Sept, v 41, No 2, 215-17, 8 coloured figs on 1 pl

Hitherto, evidence of the consumption of haemoglobin by malaria parasites has been derived from studies of (1) the pallor of infected red cells, (2) the formation of malarial pigment and its identification with haematin, and (3) respiration of plasmodia in monkeys.

The present author bases his study on the staining reaction of cyanol with haemoglobin in thin blood films containing malaria parasites, obtained from human and animal sources.

Cyanol (colour-index 715) in the reduced and colourless state, is oxidized in the presence of haemoglobin, which it stains blue. The author applied to blood films the method of staining haemoglobin in sections described by DUVV [this *Bulletin*, 1946, v 43, 1081], thus resulted in the washing out from red cells of the blue-stained haemoglobin, as Dunn's working reagent was found to be too acid for films.

The following procedure was therefore evolved —

Dunn's stock solution is prepared by dissolving 1 gm of cyanol in 100 cc of distilled water and adding 10 gm of zinc powder (C P) and 2 cc of glacial acetic acid, the mixture is boiled and quickly loses its blue colour.

The working stain is prepared immediately before use and consists of 5 cc of filtered stock solution (which has been kept over the zinc) and 0.5 cc of 3 per cent hydrogen peroxide.

As a counterstain, either 1 per cent aqueous safranin or diluted Leishman's stain was used. The different species of plasmodia showed distinctive staining with safranin, e.g., *P. gallinaceum* stains pink, while *P. vivax* is much lighter in colour. With Leishman's stain, there is no eosinophilic staining of the red cell, which remains cobalt green.

With the above methods, normal red cells stain cobalt green, parasites stain variously, e.g., pink (with safranin in *P. gallinaceum* infections), a faint-brownish yellow (with safranin and *P. vivax*), or blue-red (with Leishman's stain in *P. vivax* and *P. falciparum* infections). Safranin stains nuclei of fowl red cells a warm yellow-brown, malarial pigment, although prominent, apparently does not react with cyanol under the conditions described.

Young forms of parasites did not show any apparent loss of cyanol-staining material in the containing red cells, large rings showed a loss of green colour from their immediate neighbourhood. With amoeboid forms, the containing red cell showed only a little green colouration, the remaining green was distributed irregularly through the cell and was seen in the area not immediately in contact with the parasite. In *P. gallinaceum* infections, where there is little amoeboid activity, the green stain was absent only from the part of the cell occupied by the parasite.

Little if any, staining with cyanol was shown by red cells containing fully grown parasites such as *P. vivax* or *P. falciparum* gametocytes and *P. knowlesi* schizonts.

[All these forms are clearly shown in eight figures on a coloured plate.]

The usual appearances described in relation to infected red cells stained by the common methods are discussed, together with past views on the reduction of colour in red cells infected with malarial parasites. The author concludes, from the experiments described, that the actively amoeboid and more slowly growing parasites use the haemoglobin from most of the red cells, while the relatively inactive species merely use that in their immediate neighbourhood.

H J O'D Burke-Gaffney

MACDOUGALL, Mary S. Cytological Studies of *Plasmodium* the Male Gamete. *J. National Malaria Soc.* 1947 June, v 6, No. 2 91-8, 18 figs. on 5 pls. [37 refs.]

The study of the production of male gametes of *P. vivax* and *P. falciparum* has shown the author that chromosomes appear in the procoxa. The films were wet fixed and stained by Giemsa or haematoxylin. The earliest stage is that of four granular bands which are followed by four pairs of chromosomes arranged in a row. Next there occur two parallel bands which can be described as the pachytene stage. At this stage, the male gametes begin to form and four pairs of chromosomes are differentiated from the pachytene stage. Only one paired mass of chromatin enters each male gamete but each may represent more than one pair of chromosomes. When fertilisation occurs, the male gamete with its pair of chromosomes enters the female gamete. In some cases sterile male gametes are formed without any chromatin and it seems that in certain strains of parasite these sterile males preponderate. In such cases mosquito infection is difficult. There are many gaps in the cycle and further studies are in progress. The paper is illustrated by a series of micro-photographs and line drawings.

C. M. H. Cryan

BART, B. C. Abnormal Development of Malarial Oöcyts in *Anopheles stephensi*. *Indian J. Malariology* 1947 Mar v 1 No. 1 129-32, 3 pls.

Three abnormalities were noticed in malarial oöcyts in the gut of artificially infected *Anopheles stephensi*. The black spores of Rose were found in 2 of 173, 13 of 354 and 4 of 61 mosquitoes fed on *P. vivax falciparum*, and malarial carriers respectively. In *falciparum* infections, oöcyts were occasionally found in the lumen of the gut instead of in the outer layer and it is concluded that such mosquitoes would not become infective. The third abnormality was seen in a *vivax* case where twin oöcyts occurred, probably as the result of two zygotes settling down close together.

P. C. C. Garnham

PERE, F. Die Stechmücken und ihre Bekämpfung. Teil I. Die Fiebermücken des Mittelmeergebietes. [Mosquitoes and their Control. Part I. *Anopheles* of the Mediterranean Region.] *Hyg. Zool.* Leipzig 1942, v 8, 150 pp. 170 figs. & 2 folding keys. [15 refs.]

The author has produced a general summary about the *Anopheles* of the Mediterranean region which is, at least in most respects, accurate and well illustrated. It would be suitable for a man who was to practice hygiene in that area, assuming that he had a slight general knowledge of entomology.

The introduction, which runs to about sixty pages, gives the characters of the genus *Anopheles* and the external anatomy of these insects with special reference to points used in determining species. The larger and more special part of the work deals with the Mediterranean species. The geographical limits of the region are defined in such a way as to exclude Persia, which is perhaps unfortunate. The author then gives a list of the species known to occur in the region, with lists of those found in the separate countries. This is followed by an account (generally two or three pages with text figures) of each species, with its diagnostic characters, geographical distribution, biology and importance in relation to malaria. The total number of species in the region is given as twenty counting *A. maculipennis* as one but the author points out that many of these are found only in a very limited part of the region, but that eight are of fairly wide distribution within it. One observes a few points on which the expert would disagree with the author—for instance it is



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stated that *A. superpictus* occurs in Spain and Portugal, which is probably an ancient error based on a misidentification. The work is concluded with keys to the adult and last larval stage, and with a list of principal books and monographs, which does not seem to have been very well selected. P A Buxton

MARAL, A D F & PENIDO, H M. Distribuição dos anofelinos no Vale do Rio Doce (Percurso da E F Vitória a Minas) Espécies Transmissoras da Malaria. [Distribution of Anophelines in the Neighbourhood of the Rio Doce] Rev Serviço Especial de Saúde Pública Rio de Janeiro 1947, v 1, No 1, 163-78, 1 map English summary

Studies of species of anophelines were made along a part of the Vitória-Minas railway which runs from Vitória on the coast of the State of Espírito Santo to Presidente Vargas in Minas Gerais. During 1943, 544,938 anopheline larvae and 10,973 adults were captured in human dwellings, an additional 1,022 adults were captured out of doors. Dissections of 1,118 stomachs and salivary glands indicated that *Anopheles darlingi* and *A. albitarsis* were naturally infected and were the vectors of malaria in that area. Infections were found in the stomachs of 75 per cent of 781 *A. darlingi* examined and 13 per cent of 226 *A. albitarsis*. In 7,094 blood films examined, malaria parasites were found in about 5 per cent. *P. falciparum* accounted for about one-half of these. Details of these figures and of species distributions are shown in seven tables. H J O'D Burke-Gaffney

WEXLER, L, ADAMS, H V & GOLDBERG, L C. The Accidental Appearance of Quartan Malaria in a Therapeutic Malaria Treatment Center Amer J Syph 1947, Sept, v 31, No 5, 518-21, 2 figs

Quartan malaria is rare in the United States. The authors record the case of a Negro soldier, aged 36, admitted to a hospital in Augusta, Ga, for treatment of neuro- and cardiovascular syphilis. Fourteen days after admission, the patient complained of backache, joint pains and myalgia. His temperature exceeded 102°F that evening, fell to normal next morning and rose to 101°F in the afternoon. A blood smear was negative. For several days, a quotidian type of hyperpyrexia continued. On the 10th day of the fever (during which daily blood examinations had been made) quartan malaria parasites were found in the patient's blood. The malaria was terminated by treatment with chloroquine (S N 7618).

The origin of the infection is discussed. The patient was born in Alabama, and except for yearly visits to Panama City, Florida, between 1931-1940, had not left there until he entered the army in 1944. Thereafter, he served in Wyoming and Massachusetts and later in Europe (England, northern France, Luxembourg and Germany) until November 1945. On returning to the United States he lived for some weeks in Arizona and thereafter in his birthplace, Birmingham, Alabama. Nothing in his history could be attributed to malaria and he had never had any blood transfusions. The hospital ward to which he was admitted was a therapeutic malaria ward, where quartan and tertian strains were used. It was well screened and sprayed each month with residual DDT. As the patient had been receiving bismuth injections, the possibility of syringe or needle transmission was considered and abandoned, though it is added that frequent use and exchange of syringes and needles takes place, because of routine penicillin therapy, however, sterile technique was always used.

Malaria is widespread in the south-eastern States, but the quartan parasite has "an unexplained spotty distribution". A delayed onset or a relapse of a

previous autochthonous infection was not found to be wholly compatible with the patient's history the final possibility is therefore considered that transmission was by an anopheline from a patient receiving therapeutic quartan malaria. Inspection proved the presence of *Anopheles quadrimaculatus*, *A. punctipennis* and *A. crucians* less than 850 yards from the hospital. It is stated that the incubation period of mosquito-induced quartan malaria varies from thirty to forty-nine days, yet exceptions may prove the rule, as in this reported case."

The authors re-emphasize the need for screening wards inhabited by patients receiving therapeutic malaria, and for providing mosquito nets where anopheline vectors are known to occur locally: a conclusion already drawn by MARSH and YOUNG (*Venereal Dis. Information* 1941 v. 22, 271). Strict asepsis is essential in such wards, since the possibility that this reported infection might have been introduced through syringe or needle cannot be completely dismissed.

H. J. O'D. Burke-Gaffney

HORRIG R. O. Induced and War Malaria. *J Trop. Med & Hyg.* 1947 Aug., v. 50 No. 8, 150-59 8 figs.

This paper records the experience of a bridge-construction party of the German army 214 strong none of whom had been previously exposed to malaria. In the summer of 1941 they were near Larissa in Greece. 116 contracted malaria—112 *P. vivax* infections, 2 *P. falciparum* and 2 mixed. Ninety-six of the benign tertian cases were followed up. 74 relapsed. The total number of relapses was 159. The author compares the results of his observations with the 161 cases of induced *P. vivax* malaria reported by JAMES and NICOL in 1932 (quoted from *Discussions* reviewed in this *Bulletin* 1933 v. 30 76). The similarities are striking and confirm James's opinion that there are no great differences between induced and naturally acquired infections. The relapse rate was, however, much higher in the author's cases than in those reported by James. The author believes that tendency to relapse is associated with the massiveness of infection. A multiplicity of infective anopheline bites may result in infection with heterogeneous strains.

A graph shows the number of patients that suffered 1, 2, 3, 4, 5 or 8 relapses. The decline is in the nature of a simple exponential curve, which would also express the chances of the individuals receiving no, one, two, three or more infective bites.

The cases studied indicated that the longevity of *P. vivax* once the parasite has entered the body in its endo- or exo-erythrocytic stages, with or without atelarin treatment, overt or subclinical, lasts one and a-half years and no longer.

Norman Whit

BIANCO A. A. SAUNDERS, G. M. LEVINE A. S. & CONY R. Long Term Observation of *Plasmodium vivax* Malaria in the Returned Serviceman. Parts II & III. *U.S. Nav. Med. Bull.* 1947 May-June & July Aug. v. 47 Nos. 3 & 4 550-67 753-65 5 figs. [27 refs.]

There is a general impression that *P. vivax* malaria acquired in the South Pacific has a special tendency to relapse over very long periods. Many patients exhibit such a tendency but many others have suffered only one to four relapses during two years, though the place and degree of exposure to infection were identical with those of the group of chronic relapses who suffered up to 20 proved relapses. The future clinical course of malaria appears to be determined by an unknown clinical factor or factors. Repeated relapses have also been known in patients who acquired infection in the Caribbean, Mediterranean and China areas.

In patients observed personally in two or more relapses who had been out of endemic malaria areas and off suppressive mepacrine for more than a year, there was a lengthening of the period between relapses. These patients began to tolerate malaria a great deal better, the attack produced only mild discomfort and responded to very small amounts of antimalaria therapy. Spontaneous remission may occur. But occasionally a severe relapse will occur 3 years after exposure to infection, this is, however, very exceptional.

Numerous expedients were tried to precipitate relapses, all failed. They included erythema doses of ultraviolet light, deep X-ray therapy to the spleen, adrenaline subcutaneously, a course of desoxycorticosterone injections, infusion of 1,000 cc of physiological saline solution via the spleen, diathermy to the spleen for 7 days, immersion in an ice-cold bath to the limit of tolerance, penicillin in maximum dosage, calcium pantothenate, 45 grains daily for 7 days, ketogenic diet with 60 grains of ammonium chloride daily for 7 days, exposure in a pressure chamber, equivalent to 18,000 feet altitude, for five hours, gradually increasing insulin up to 100 units daily, for 14 to 21 days, with periods of hypoglycaemia of 3-4 hours before administration of dextrose, most strenuous exercise.

For treatment, atebryn [mepacrine] is superior to quinine. The officially recommended total dosage, 2.8 gm in 7 days, is effective and nothing is gained by increasing the dose. Where prompt return to duty is imperative, the "flash" treatment may be useful. The patient receives simultaneously 0.4 gm atebryn intramuscularly and 0.2 gm orally, followed by 0.2 gm orally every 4 hours, for 3 doses, a total of 1.2 gm in 12 hours. This is followed by 0.1 gm a day as long as the patient remains in an endemic area, or for 10 to 16 days if on duty in a non-endemic area. This régime compared favourably with the 7-day standard treatment, within 48 hours the patients were ambulatory.

Seventeen patients were treated with plasmoquine-quinine, there was only one relapse during a 120 days' observation period, much the best result obtained with any treatment.

Chronic headache was the most frequent residual symptom which followed treatment of an acute relapse. An extensive electro-encephalographic study was made of these headaches. The qualitative and quantitative electro-encephalogram findings in headaches occurring in chronic recurrent malaria and in headaches unaccompanied by any recognized disease process involving structural changes were almost identical. This indicates that malaria headaches are not an integral part of the malaria infection.

Part III of this paper deals with neuropsychiatric problems in patients suffering from recurrent *vivax* malaria. Psychogenic illness was found to be no different in nature or in frequency in these patients than in a non-malaria group of patients. In each case of mental illness, total personality studies are indicated, malaria is only another incident in the total environment of the personality under study.

Norman White

MATEO ALONSO, A. Estudios sobre los cuadros clínicos mas graves del paludismo [Clinical Study of the Severer Forms of Malaria] XII Conferencia Sanitaria Panamericana Cuadernos Amarillos Publicaciones de la Comisión Organizadora No 22 Caracas 1946, 74 pp., 3 graphs & 9 figs [Bibliography]

The first part of this article treats of the cerebral forms of malaria. The author's remarks are based on cases which occurred during an epidemic in 1945. In the latter half of the year, 194 cerebral cases were seen, 152 of them first attacks. One hundred and eighty-seven were children between 6 months and 5 years of age, the other seven were respectively 3 of 6 years and one each of

7 9 13 and 20 years. Of the 152 first attacks 84 were in males 68 in females 18 died, 11 boys and 7 girls. A more detailed table of cerebral symptoms shows that of the 194 there were 56 with signs of meningitis, 43 with status epilepticus, 32 with fits of an epileptic type, 28 of coma, 19 with fits apoplectic in type and 16 with symptomatic epilepsy. General remarks are made on these and four cases are detailed. [Attempts have been made to illustrate them by photographs, but all are out of focus and unrevealing.] The last few pages are devoted to discursive remarks on the possible effect of sunlight in the causation of blackwater fever  
H. Harold Scott

BOONK, C. Malaria haemorrhagica. [Haemorrhagic Malaria.] *Med. Maandblad Batavia*. 1947 July No. 12, 223-4

The English summary appended to the paper is as follows —

Description of two typical cases of haemorrhagic malaria with severe haemorrhages from the bowel and in one case epistaxis, in the other case haematemesis. Both patients showed a few purpuric haemorrhages into the skin. Large scale blocking by parasite-containing blood corpuscles of capillaries of the intestinal canal as well as of the brain and other organs was present. There were no signs of complicating diseases.

TEMEKIN, M. La pathologie et la thérapie de l'hémoglobino-paludisme. [Pathology and Treatment of Malarial Haemoglobinuria.] *Rev. Paludisme et Méd. Trop.* 1947 Oct. 15, v. 5, No. 41 239-41

MOONENBOUT DUMADIE, M. & SARAKER, N. La forme aiguë de l'anémie splénique hémolytique de paludisme. [Hyperacute Haemolytic Splenic Anaemia in Malaria.] *Rev. Paludisme et Méd. Trop.* 1947 Oct. 15 v. 5, No. 41 233-8.

NELSON, M. G. Serological Tests for Syphilis in treated *Plasmodium falciparum* Malaria. *Trans. Roy. Soc. Trop. Med. & Hyg.* 1947 Sept. v. 41 No. 1 127-32.

The author discusses the literature on the false positive serological tests for syphilis which sometimes occur in sera from persons having malaria. These results particularly require recognition in persons suffering concurrently from non-syphilitic, venereal disease and malaria, in whom latent syphilis might be suspected.

At the R.A.F. Hospital, Takoradi, Gold Coast an investigation was made by the author on the sera of 200 Europeans suffering from acute *Plasmodium falciparum* infections. The cases constituted unselected consecutive admissions in all degrees of clinical severity in whom syphilis was excluded by all possible methods. All patients received full anti-malarial treatment upon diagnosis.

Blood was taken within 24 hours of the finding of the parasites and again on the 10th day after the first paroxysm. The sera were tested in parallel against the Ide, Mehncke and Kahn antigens. Positive sera were subjected to the Kahn verification test.

The results of different stages are shown in four tables. False positive results were found in about 3 per cent. of cases, the three tests being in satisfactorily close agreement (Ide 2 per cent., Mehncke 4 per cent., Kahn 3 per cent.). The author refers to the comparable investigation by ELKINS and FINDLAY in 80 patients in West Africa [*Bulletin of Hygiene* 1945 v. 20 254] these workers found 23 false positive results with the Kahn and 4 with the Ide test.

The present author found the Ide test a useful slide method which correlates fairly well with the Kahn reaction. He shows in a table the results of 1,000 sera tested in West Africa against the three antigens in parallel in primary and

treated syphilis, the Meinicke was the most sensitive test and the Ide the least. In the few secondary cases examined, agreement was complete: no non-specific reactions occurred in cases of non-syphilitic venereal disease. The percentages of positive results were, Ide 49, Meinicke 80.4, Kahn 65.4. Discrepant results were found in the sera of 200 healthy Africans examined for evidence of latent yaws or syphilis: the percentages of positive results were, Ide 28, Kahn 37, Meinicke 48.5.

The author considers the Meinicke to be the most sensitive flocculation test under tropical conditions.

False positive results in treated malaria occurred in the first 14 days, and sera were negative, in those followed up, within 40 days of the first paroxysm. The author quotes KITCHEN *et al.* [*Bulletin of Hygiene*, 1939, v 14, 619], who found most of the false positives between the 15th and 21st days: the results remained positive for 2 months. He also refers to the work of DAWBER [this *Bulletin*, 1944, v 41, 364]: the optimum time for obtaining false positive results is later in untreated than in treated malaria and the sero-positivity lasts longer.

False positive results due to malaria can be distinguished from true syphilitic reactions by (1) serological follow-up and (2) verification tests. Since malarial false positives only persist for about 1 month in treated cases and 2 months in untreated ones, follow-up for 2 months after full anti-malarial treatment should allow of a differential diagnosis. The author did not find that either the Kahn verification test or the Richardson potentiation test could be relied upon in the tropics to distinguish true from false positive reactions due to malaria.

The author notes the difficulty of achieving serological specificity in areas where yaws is endemic: in any case even where syphilis and yaws can be excluded, certain other factors affect the interpretation of false positive results, of which the following are important:—

- (1) *P. vivax* gives more false positives than *P. falciparum* [KITCHEN, *loc cit.*]
- (2) The results vary in the different clinical stages of the disease [KITCHEN, DAWBER, *loc cit.*]
- (3) Anti-malarial treatment results in fewer false positives than occur in untreated cases: and these results occur earlier (2 weeks) in treated malaria than in untreated cases (3rd week).
- (4) Results on the same sera vary greatly with the test employed: on the whole, the Wassermann reaction is more sensitive to false positive sera in *P. falciparum* malaria and the Kahn test in *P. vivax*.

[For a discussion of false positive tests, see the review of Serum Tests for Syphilis, by T. E. OSMOND, *Bulletin of Hygiene*, 1946, v 21, 627.]

H. J. O'D. Burke-Gaffney

CHINN, M. Nouvelle enquête sur les seroreactions de Bordet-Wassermann et de Kahn dans la malaria. [A New Study of Wassermann and Kahn Reactions in Malaria] *Ann. Soc. Belge de Méd. Trop.* 1947, Mar 31, v 27, No 1, 5-15.

The author, working in the Medical Laboratory at Coquilhatville, was prompted to make this study as a result of finding strongly positive WR and Kahn reactions in a European during an acute attack of malaria. Syphilis could be excluded clinically and the patient's serological tests had been negative a few weeks earlier.

After discussing British, American and Belgian workers' views on biological false positive reactions in malaria, the author describes tests made by himself on 265 African children, between the ages of 1 and 13, in whom syphilis could

paludrine (250 mgm. t.i.d.) there was a clearance of the blood parasites in less than 2 days. Pamaquin given alone (0.01 gm. t.i.d.) was followed by parasitaemia for 31 days.

The following changes were observed in the asexual cycle of the parasites with all drugs: (1) slowing down of rate of development of the various stages; (2) tendency of large ring and amoeboid form to "collapse"; (3) bunching together of pigment; and (4) destruction of one or more of the parasite stages in the asexual cycle.

The following changes were attributed to the specific drug taken. *Quinine* had a rapid action. The maximum killing effect seemed to be exerted on merozoites and the youngest trophozoites. *Mepacrine* also had a rapid action. A collapse of amoeboid trophozoites, bunching of pigment and destruction of schizonts occurred. A single dose of 0.2 gm. given by intramuscular injection at the pre-schizont stage usually caused a rapid clearance of parasites and had a lethal effect on the schizonts. *Pamaquine* was a slow-acting drug. It was schizonticidal and active in its effect on merozoites [merozoites are red cells containing merozoites]. Sometimes extrusion of pigment was caused before the parasite matured. The author believes that it is this liberation of pigment which results in the occurrence of a clinical malarial paroxysm. The powerful schizonticidal action of pamaquin is perhaps not widely recognized and it is noteworthy that the daily dosage of the drug (30 mgm.) is 20 to 30 times smaller than that of mepacrine required to produce an equivalent result. *Paludrine* acted on the early schizonts and interfered with chromatin division. The forms which were produced persisted, and resembled female B.T. gametocytes. *Paludrine* did not clear the blood of benign tertian gametocytes.

Patients were followed up for a minimum period of six months, many of them for longer. In all, 450 cases were followed up. Of every 10 who had relapse infections and were treated with quinine and pamaquin for 10 days, 8-9 were cured. The relapse rate in patients from the Far East treated with 250 mgm. of paludrine plus pamaquin 0.01 gm. t.i.d. were also low though these drugs together proved toxic. In more than 200 patients to whom pamaquin was given at some stage of the illness, the relapse rate was significantly lower than in those to whom other drugs, but no pamaquin, were given. A series of 50 patients with multiple B.T. relapses treated with an intermittent dosage of quinine plus pamaquin over a period of 30 days did not relapse in one single instance.

[This paper reviews the experiences of a team working on infections produced by at least two strains or varieties of *P. vivax*. This is a factor which must always be remembered when various régimes of treatment are compared. In the main, the findings are similar to those of previous workers on this subject. Many of the cases were drawn from a population taking suppressive mepacrine but no indication is given about the regularity of its administration. There is no direct suggestion that the strains in this (Mediterranean) area were resistant to mepacrine. Little support will be found for the assertion that malarial parasites released at schizogony or as the result of treatment is responsible for the relapse paroxysm. The results obtained with the group consisting of returned soldiers of war from the Far East should be considered with reserve as here considerable degree of immunity must have been present. Some of the statements warrant adequate documentation before comment can be made.]

Robert H. Black

DR. M. N. & DUTTA, P. N. A Clinical Study on Paludrine. *Indian Med. Gaz.* 1947 May v 82, No. 5 257-60.

Fifty-eight patients admitted to Medical College Hospital, Calcutta, with active malaria and parasitaemia were treated with paludrine [presumably

orally] Twenty of these had M T infections and the remainder B T , none had recently had any other antimalarial treatment. The blood was examined for parasites every 24 hours. Patients in Group I (4 M T and 8 B T ) were given 1 " tablet " [200 mgm ] of paludrine thrice daily for 7 days and then twice daily for another 7 days. " Parasites " [presumably asexual] vanished from the blood within from 48 to 96+ hours and the temperature dropped to normal within from 12 to 80 hours in these cases. Group II patients (6 M T and 14 B T ) were given 1 " tablet " thrice daily for 7 days. In these cases ' parasites ' vanished from the blood in from 24 to 72+ hours and the temperature subsided within from 12 to 96 hours. Group III patients (1 M T and 13 B T ) received 1 " tablet " twice daily for 7 days. " Parasites " vanished from the blood in from 24 hours to 72+ hours, and the fever subsided within 24 to 72 hours in all but two cases (both B T ) in which it persisted for 120 hours.

Group IV cases were all severe, with very heavy parasitaemia (4 M T and 3 B T ). These received 2 " tablets " thrice daily for 2 days, and then 1 " tablet " thrice daily for 5 or 6 days. Those patients who were too ill to swallow the tablets were given them, crushed and suspended in fluid, through a nasal tube. In these cases the " parasites " vanished in from 48 to 72+ hours, and the temperature subsided within 24 to 84 hours.

Group V cases, five in number, were not treated personally by the authors, and received 1 " tablet " thrice daily for 3 days. [No data are given relative to these.]

No toxic effects from the treatment were observed in the 58 cases, and no relapses were encountered within an observation period of 2 to 3 weeks. The authors consider that paludrine is an effective drug and that " so far it appears to hold out fair prospects of being effective against relapse ", but [wisely] add that the period of observation is inadequate to justify a final conclusion on this matter.

A R D Adams

CHAUDHURI, R N & RAI CHAUDHURI, M N Clinical Trials of Paludrine.  
*Indian Med Gaz* 1947, May, v 82, No 5, 247-53, 9 figs

Eighty patients (chiefly Indian) admitted to the Carmichael Hospital, Calcutta, suffering from acute malarial attacks of less than a week's duration, who had " fair " or " large " numbers of parasites in their blood, and who had not received antimalarial treatment prior to admission, were treated with paludrine orally. Forty-seven of these had *Plasmodium falciparum*, 30 *P. vivax*, 2 *P. malariae*, and 1 mixed *P. falciparum* and *P. vivax* infections. The dosages employed were as follows —

Age in years	Above 12	6 to 12	Under 6
Regime A	100 mgm (1 tablet)	50 mgm ( $\frac{1}{2}$ tablet)	50 mgm ( $\frac{1}{2}$ tablet)
Regime B	300 mgm (3 tablets)	150 mgm (1 $\frac{1}{2}$ tablets)	100 mgm (1 tablet)
Regime C	(1 tablet t d s for 4 days)	( $\frac{1}{2}$ tablet t d s for 4 days)	( $\frac{1}{2}$ tablet b d for 4 days)

All became afebrile and free from asexual parasites within, at most, 5 days (full data are given in figures, charts and tables).

The average periods within which the temperatures became normal and the asexual parasites disappeared from the peripheral blood after treatment were as follows —

Regime	Duration of fever	Duration of asexual parasites in blood
A	3 days	2-6 days
B	2-4 days	2-4 days
C	2-3 days	2-3 days

In those treated under régime A (7 M.T. 2 B.T. 1 Q. and 1 mixed M.T. and B.T. infections) asexual parasites had vanished in 82 per cent. and the temperature had fallen in 73 per cent. of the cases within 3 days. Under régime B (28 M.T. and 16 B.T.) these results were achieved in 88 per cent. and 88 per cent. and under régime C (14 M.T. 12 B.T. and 1 Q.) in 93 per cent. and 89 per cent. respectively.

There was evidence of more rapid action of the drug in *P. falciparum* infections than in those due to *P. vivax*; gametocytes of neither species were destroyed by the drug, but mosquitoes fed on two patients with gametocytes (*P. falciparum*) 4 or 5 days after treatment did not become infected. The relapse rates in 39 patients (24 M.T. 12 B.T. 2 Q. and 1 mixed M.T. and B.T. infections) observed for 2 to 4 weeks after treatment were high, especially among the cases of M.T. malaria treated with régime A or B, none (8 M.T. 2 B.T. and 1 mixed M.T. and B.T. infections) of the 39 patients treated with régime C relapsed within these periods of observation.

The authors conclude that paludrine has an action on clinical malaria comparable with that of quinine or of mepracrine. A dosage of 100 mgm. of paludrine thrice daily for 4 days is more effective than either a single dose of 100 mgm. or one of 300 mgm. in arresting an acute attack of malaria. No untoward effect was observed in any patient which could be attributed to the drug.

A. R. D. Adams

PATEKH J. G. & BOGHIANI B. P. Clinical Trial of Paludrine in Malaria. *Indian Med. Gaz.* 1947 May v 82, No. 5 253-5.

Fifty patients admitted to the Sir J. J. Group of Hospitals, Bombay, suffering from acute malaria infections were treated with paludrine (presumably orally) after at least one rigor had been observed in each case. These were made up of 26 cases of B.T. 20 of M.T. and 3 of Quartan malaria; there was 1 mixed M.T. and Q. infection.

The dosages of paludrine employed were (1) 100 mgm. (single dose) (2) 300 mgm. (single dose) (3) 100 mgm. daily for from 2 to 8 days (4) 100 mgm. once weekly for from 2 to 24 weeks (5) 100 mgm. thrice daily for from 2 to 10 days and (6) 200 mgm. thrice daily for from 3 to 5 days. In most of the cases treated, even those with a single dose of 100 mgm. (7 B.T. and 3 M.T.) the dosage was effective in arresting the paroxysm usually within 24 hours, but sometimes it took longer (in a case of M.T. getting 100 mgm. weekly asexual parasites persisted for 6 days and the fever for 9 days after the first dose of the drug). Two persons suffering from M.T. malaria died of cerebral complications within 4 hours and 6 hours, respectively, of receiving each a single dose of 300 mgm. of paludrine. In 43 of the 50 persons treated asexual parasites vanished from the peripheral blood, usually in 1 to 3 days after the start of treatment. Gametocytes of all three species, often in increased numbers, persisted in the blood for from 4 to 20 days (and in a case of B.T. infection for 90 days) after treatment. Among 25 patients followed up for 3 weeks to 9 months (15 B.T. 7 M.T. 2 Q. and 1 mixed M.T. and Q.) after the various treatments there were 7 relapses; these occurred in 1 of 3 M.T.



cases treated with a single dose of 100 mgm (these were followed up for at least 4 months), in the only B T case treated with 100 mgm daily for 8 days (followed up for 3½ months), in 4 of 6 B T cases treated with 100 mgm weekly for from 2 to 24 weeks (followed up for from 5 to 9 months), and in 1 of 2 B T cases treated with 100 mgm thrice daily for 3 days (followed up for from 5 to 7 months) Data relative to the dosages, types of infection and subsequent history of the patients are given in a table

Six patients were considered to have shown toxic manifestations due to the drug, but these were unrelated to the size of the dosage, and were attributed to personal idiosyncrasy to the drug The manifestations included weakness and drowsiness, diarrhoea and vomiting, pains in the back and urticarial eruptions with desquamation The authors, on their results, consider paludrine at least equal, if not superior, to other antimalarials in the clinical cure of malaria

A R D Adams

1 BULL U S ARMY MED DEPT 1947, Oct, v 7, No 10, 834-5 **Chloroquine-Diphosphate—a Newly-Standardized Antimalarial Drug**

11 — pp 835-7 **Clinical Evaluation of Chloroquine**

1 Successful results in the United States and elsewhere with the antimalaria drug chloroquine (SN 7618) have already been reported [this *Bulletin*, 1946, v 43, 708, 1011, 1947, v 44, 502, 792] The Medical Department of the U S Army has now adopted this product as a standardized "improved malarial therapeutic and suppressive drug" It is dispensed as tablets of 0.5 gm, equivalent to 0.3 gm of base The nature and effects of the drug have already been described in the abstracts quoted above It is noted that the standard dosage adopted for the initial attack or an acute relapse is one 0.5 gm tablet, followed 4 hours later by a second, this dose of 0.5 gm being repeated at 9 a.m. next morning and at the same time on two further days A total dosage is thus given in 4 days of five 0.5 gm tablets (2.5 gm) containing 1.5 gm. active base This dosage should not be exceeded As a suppressive, a single dose of one 0.5 gm tablet is given weekly

With this schedule, the attack is usually controlled promptly and the parasites removed from the blood in less than 24 hours The interval between relapses is considerably longer than when quinine or mepacrine is used Signs of toxicity are few, mild and rarely require discontinuance of the drug The only troublesome manifestation noted with frequency of any significance was pruritus without rash in less than 10 per cent of patients treated Anorexia, mild nausea and vertigo occurred but were rare The announcement adds that the removal of atabrine [mepacrine] from the list of standard items is not contemplated at present

11 This report records the results of clinical trials of chloroquine on 1,322 patients in U S Army hospitals, under standardized conditions *P. vivax* was present in 1,277, *P. malariae* in 44, and one patient was treated on clinical findings only No *P. falciparum* infections are included Data regarding previous attacks treated with other drugs were available in 896 cases Of these, 90 per cent had suffered from one or more relapses Sixty-five patients had had relapses after previous treatment with chloroquine, 54 of these occurred after a single treatment only In 1,077 patients of whom the relevant data were available, 5 per cent were afebrile on admission, 64.6 per cent became afebrile within 24 hours, 23.7 between 24 and 48 hours and 6.6 per cent after 48 hours In 700 patients, it could be recorded that 59.7 per cent became free of parasites within 24 hours, 29 per cent between 24 and 48 hours, and 8 per cent between 48 and 72 hours The remaining 2.7 per cent did not become parasite-free until after 72 and under 96 hours Of all the 1,322 patients,

21.4 per cent. showed one or more reactions attributable to the drug. Pruritus accounted for 124 of these reactions, anorexia for 86, vertigo or tinnitus for 78, diarrhoea for 33 and urticaria and malaise for 4 and 3 respectively. [Even though they were generally mild and rarely required discontinuance of the drug reactions attributable to the drug to the extent of 21 per cent. do constitute an undesirable feature.]

H J O D Burke-Gaffney

KAMAL, A. M & ARDEL MESSIRI, G. Aralen. A New Antimalarial Compound, SN 7618. Reprinted from *J Egyptian Pub. Health Ass.* 1947 Apr 31-6.

The authors record a clinical study of Aralen (the Winthrop Products trade name for chloroquine SN 7618) on similar lines to that previously reported, also from Egypt by HALAWANI *et al.* [*this Bulletin* 1947 v 44 792]. The drug was administered to patients in the Damanhur and Tanta Fever Hospitals in two schedules. The study was confined to new attacks, not relapses. Aralen is supplied in 0.25 gm. tablets. Schedule A consisted of an initial dose of 1 gm. (4 tablets) followed by 0.5 gm. six hours later and again after a further 24 and 48 hours. Thus 2.5 gm. (10 tablets) were given in 3 days.

In Schedule B 2 gm. (8 tablets) were given in equal doses of 0.5 gm every 4 hours.

Forty five patients (39 benign and 6 subtertian infections) were treated on Schedule A. In 35 of the benign cases treatment was given in a morning afebrile period in expectation of an attack. In 22 of them, the attack occurred in the afternoon, but the temperature returned to normal next morning and remained thus until the patients were discharged 12 days later. In 13, the attack was prevented and no subsequent attacks occurred. In the remaining four treatment was given when the temperature was raised—in all, it dropped to normal in 12-24 hours, but a second attack occurred within a further 24 hours. In 33 per cent. of the cases, therefore the normal temperature was maintained, and in all the cases, cure of the acute attack occurred within 24-48 hours.

In the 6 subtertian cases, one patient maintained the initial normal temperature, 2 became normal in 24 hours, 2 between 24 and 48 hours and one within 72 hours.

Eight patients with benign tertian malaria were treated on Schedule B. Of these, 4 maintained their initial normal temperatures, 3 became normal in 24 hours and one suffered an attack the next day. Thus, acute clinical attacks were cured within 24 to 48 hours in almost every case whether the drug was given on one or over 3 days. This is considerably shorter than the time required for treatment with quinine or mepracine.

In a table the authors compare their results with American experience of mepracine and Aralen which indicate that their own findings in the case of the latter drug in respect of its effect on temperature correspond fairly closely with the American experience [the American experience on which these figures are based is not indicated].

In studying parasite clearance the blood of 28 patients under treatment with Aralen was examined twice daily for 12 days. In benign cases on Schedule B trophozoites and gametes (sic—evidently gametocytes) disappeared from the blood of the 8 patients concerned within 48 hours of treatment. In 15 patients on Schedule A, only 5 were negative in 48 hours, 7 became negative in 72 hours and 3 after 96 hours. Thus only 33 per cent. of patients were free of parasites within 48 hours compared with 96.3 per cent. in the American experience. It is, however emphasized that all the 8 patients on Schedule B became parasite-free in 48 hours.

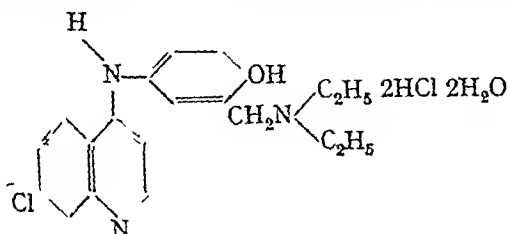
In subtertian infections (numbers not stated, but presumably 5), trophozoites disappeared within 72-96 hours, but gametes were not affected.

Only 8 patients in the whole series were followed up no relapses were noted at the time of writing (20 to 48 days). There was very little toxicity in this series one patient suffered from headache and one from brief vomiting [Compare with U S Army Medical report above]

H J O'D Burke-Gaffney

SIMEONS, A T W & CHHATRE, K D Preliminary Report on a New Synthetic Antimalarial *Indian Med Gaz* 1947, May, v 82, No 5, 255-7

"Cam-Aq", 4 (3' diethylaminoethyl 4'-hydroxyanilino)-7-chloroquinoline dihydrochloride dihydrate, is a yellow crystalline powder soluble to the extent of 1 gm in 5 cc of water at 25°C Its structural formula is as follows —



This compound was found by the Parke Davis Research Laboratories to be 'several times as effective as quinine and quinacrine' in "avian malaria", absorption from the gut was very rapid and high plasma levels were rapidly reached [? in birds] The acute toxicity in laboratory animals was about that of quinacrine [mepacrine], but the chronic was one-quarter to one-half that of mepacrine Anorexia, vomiting, spasticity, clonic convulsions and respiratory failure were produced only by prolonged dosage several times greater than in the case of mepacrine The excretion of the drug from laboratory animals was slow

In view of these observations, viz, its rapid absorption, rapidly achieved high plasma level, slow excretion, low toxicity and therapeutic efficiency "in laboratory animals", the drug was considered suitable for trial in single oral dosage in human malaria, 10 mgm /kilo body weight being the dosages selected

Fifty men from the Kolhapur State Forces suffering from clinically acute malaria (39 *Plasmodium vivax* and 11 *P falciparum* infections), most of them with heavy parasitaemia were hospitalized Two-hourly temperature records were kept for the first 48 hours a tablet of ascorbic acid was given thrice daily as a placebo, a single dose of 'Cam-Aq' (10 mgm /kilo) was then given by mouth, and the blood was thereafter examined at intervals of  $\frac{1}{2}$  to 4 hours as long as parasites persisted in it In the 39 BT infections asexual parasites vanished from the blood in an average of 25 hours (max 46 hours) and in the 11 MT infections, 23 hours (max 40 hours) The fever in both infections subsided within 48 hours Circulating crescents were not obviously affected, but there was no evidence of further gametocyte formation this is ascribed to the action of the drug on the exoerythrocytic stages of *P falciparum* No relapses, clinical or parasitic, were observed among these 50 men over a period of 3 months continuous observation No toxic effects attributable to the drug were encountered among them, or among a number of non-malarial patients suffering from cirrhosis of the liver, severe anaemia, advanced tuberculosis nephritis and typhoid, to whom equivalent doses were given

Sixteen patients (10 *P vivax* and 6 *P falciparum* infections) were then treated with 7.5 mgm /kilo, and 18 (*S P vivax* and 10 *P falciparum*) with 5 mgm /kilo of the drug The results are summarized in the following table —

Dose mgm./kgm.	Number of cases		Relapses observed		Average time required for the			
					clearance of peripheral blood (in hours)		temperature to subside (in hours)	
	B.T.	M.T.	B.T.	M.T.	B.T.	M.T.	B.T.	M.T.
10	39	11	Nd	Nd	25	23	28	27
7.5	10	6	Nd	2	25.5	35	25	35
5	8	10	2	7	32.5	33	35	41

From this it is evident that the rapidity of action diminished with the dosage and that relapses occurred increasingly with the lowered dosage, particularly in the M.T. infections. The authors conclude that 7.5 mgm./kilo. is an adequate dosage in B.T. infections, but inadequate in M.T. 5 mgm./kilo. while it arrests the attack, is inadequate to prevent relapse in either infection. A few patients were given 15 mgm./kilo. with enhancement of the rapidity of action in arresting the clinical disease, but this benefit did not appear to offset its increased cost. No evidence of toxicity was noted with the bigger dose.

One hundred and ten children boarding in a Mission School Hostel suffered from much malaria, up to 20 being absent daily with microscopically diagnosed malaria. Every child in the Hostel was given a dose of Cam-Aqi (between 5 and 7.5 mgm./kilo.) within 3 days clinical malaria vanished from the Hostel and remained absent for 2 months, when the children went on holiday. On their return, two had overt malaria, probably relapses, and were treated with 10 mgm./kilo. no further cases occurred over a period of 5 months. Another 116 day boys at the school, with a similarly high malaria incidence, were given 10 mgm./kilo. of the drug. no further cases occurred over 2 months' observation. No toxic effects were seen in any of these children.

For field purposes, where it is impracticable to weigh individuals, the authors suggest the following dosages —

Infants up to 2 years	$\frac{1}{2}$ tablet	0.1 gm.
Children from 2-5 years	1	0.2 gm.
Children from 5-14 years	$1\frac{1}{2}$	0.3 gm.
Average South Indian adults	2	0.4 gm.
Tall or heavy adults	3-4	0.5-0.6 gm.

The authors consider Cam-Aqi a real advance in malaria therapeutics especially for employment in rural population.

[In the Survey on antimalarial drugs 1941-1945 edited by WISELOCKE (J. W. Edwards, Ann Arbor Michigan 1948 see this Bulletin 1947 v 44 1106) Vol. I, p. 308 and Vol. II, Pt. 2, p. 1165 may be found a description of the similar compound, S.N. 10751 with an account of its chemistry, antimalarial activity in screening tests, mammalian pharmacology and clinical investigation. For a preliminary report on Cam-Aqi see also this Bulletin 1947 v 44 698.]

A. R. D. Adams

CHRISTOPHERS, S. R. Mosquito Repellents. Being a Report of the Work of the Mosquito Repellent Inquiry Cambridge 1943-5. *J. Hygiene*, 1947 May v 45 No. 2, 178-231 6 figs. [Numerous refs.]

This is a full and well-documented survey of the whole subject of mosquito repellents, and summarizes all previous work, as well as describing the careful experiments carried out in Cambridge during the war. Previous work had been badly standardized, and, frequently impure samples of alleged mosquito

repellents had been used in which small quantities of impurities had been responsible for the effects obtained.

The author explains that it is necessary to carry out laboratory tests rather than field tests, to obtain strictly comparable results. He also stresses the importance of having a "standard insect" and gives details of methods of breeding *Aedes aegypti* for that purpose.

The paper contains detailed accounts of experiments with a very large number of different preparations containing substances alleged to repel mosquitoes, and also with a large number of pure substances. Various methods are given for making the anti-mosquito effect last under tropical conditions and when the skin is rubbed. There is an account of the effectiveness of impregnating fabrics with mosquito repellents, and a discussion of the protection given to the skin by closely woven fabrics.

Those concerned with research into the question of mosquito repellents are referred to the original paper which, although it is over 50 pages long, is still a summary of the work, and further condensation is impossible. The practical applications are as follows: Pure dimethyl phthalate is still probably the best repellent for mosquitoes and midges. It should be applied to all the exposed skin in a thin film. Creams containing dimethyl phthalate, several formulae of which are given, give good results, and a little Java citronella incorporated in the cream may keep the mosquitoes at a distance from the skin so that a complete covering is not so necessary.

Finally, the author stresses the fact that there is still much research to be done before a perfect mosquito repellent is discovered, and it should be remembered that different species of insect may react differently to the same chemical substance which may give good protection against one mosquito and little or none against another.

Kenneth Mellanby

NAGENDRA, S. Further Observations on Dry Leaf Packing for the Control of Mosquito Breeding. *Indian J. Malariaology* 1947, Mar, v 1, No 1, 67-79.

From the results of regular larval catches the author shows that there is much less mosquito breeding in portions of streams controlled by dry-leaf packing than in the sections where canalization is the sole control measure; he attributes this to the creation of a mechanical barrier against oviposition by mosquitoes. No observations were made prior to the institution of control measures, and the anopheline larvae subsequently caught were not identified. R. Ford Tredre

RAO, V. V. & RAMAKRISHNA, V. De-Weeding Tanks and Ponds in Antimalaria Operations. *Indian J. Malariaology* 1947, Mar, v 1, No 1, 51-66, 3 figs on 1 pl & 3 text figs.

In several areas in India, vector *Anopheles* breed in still water associated with aquatic vegetation such waters may be many acres in extent, rendering their control by chemical larvicides too expensive a proposition for the local villages. The obvious method of control is by removal of weeds, but the authors draw attention to the disadvantages of this, of which the principal is the production of turbidity in previously clear water, rendering it apparently unfit even for domestic purposes coincident with this is the rapid spread of the algal growth, *Microcystis*. To restore the purity of the water, the authors recommend the planting of the common aquatic herb, *Ottelia alismoides*, which inhibits the spread of *Microcystis* and limits the growth of other major plants. Manual removal of weeds may be obviated by (a) the introduction of silt-laden river water, or (b) salinification by saline waters, where these measures are

possible freshwater plants are destroyed in each case. Lastly the authors are enthusiastic about the value of raising vegetable crops on the beds of the tanks when they are dry in the summer months: the soil appears to be rendered sterile for the rest of the year and little aquatic vegetation appears when the tanks refill in the wet season.

R. Ford Treloar

BRADLEY G. H. & FRITZ, R. F. Entomological Evaluations of Results of Residual DDT Spraying during 1946. *J. National Malaria Soc.* 1947 June v 6 No. 2, 117-21

In a previous paper [see this *Bulletin*, 1947 v 44 180] the authors describe the highly effective results of residual DDT spraying as observed in some 400,000 homes in the Southern U.S.A. where the spray was applied at the rate of 100 mgm. of DDT per square foot, on one or more occasions. At this time, the authors noted that the effectiveness of DDT deposits as measured by the percentage of sprayed houses found free of live mosquitoes, gradually decreased during successive months following application. However after four months, live mosquitoes were found in only about 8 per cent. of treated houses examined. The present paper describes the continuation of this work in which, during the 1946 season, over 750,000 houses were treated but on this occasion the DDT was increased to 200 mgm. per square foot in an effort to secure a more lasting residual effect and thereby to decrease the frequency of application. A comparison of the results of the two forms of treatment are shown in the following table.

*House Inspections on Residual Spray Program*

Total treated houses inspected and per cent. free of *A. quadrimaculatus* in afternoon

Months after spraying	1946			1945*
	Number houses inspected	Houses free of <i>A. quad.</i>		Per cent. of houses free of <i>A. quadrimaculatus</i> (for comparison)
		Number	Per cent.	
-1	6,018	5,899	98.19	98.4
1-2	6,739	6,673	99.02	98.3
2-3	5,321	5,271	99.06	95.7
3-4	2,974	2,835	98.69	94.7
4+	899	883	98.22	94.2
Total	21,951	21,731		
Per cent.			99.00	97.2

BRADLEY G. H. and ROY F. FRITZ. 1946. Entomological evaluation of DDT residual spraying for malaria control. *Jour. Nat'l. Malaria Soc.* 5: 141-145.

In later table, the authors show that a greater proportion of sprayed houses found to be mosquito-positive occurred in areas with a high *Anopheles quadrimaculatus* density. During the 1946 period precipitin tests carried out in 25-98 specimens of *A. quadrimaculatus* collected on premises where the houses had been treated with DDT showed that only 40 (0.2 per cent.) gave reactions for human blood, whilst among 8,509 anophelines collected from untreated premises, 74 (1.1 per cent.) gave a similar reaction. Thus, it is indicated that the proportion of the anopheline population that had fed on human beings and survived was 82 per cent. less around sprayed than around unsprayed premises.

[This paper contains a wealth of information packed into a small space, concerning the effectiveness of residual DDT spraying on *Anopheles quadrimaculatus*, and is of particular interest in view of recently published papers by British workers on similar investigations carried out with DDT and directed against *Anopheles gambiae* in West Africa. Murhead THOMSON (this *Bulletin*, 1947, v 44, 795) in an important paper has drawn attention to the repellent action exerted by DDT when used as a residual spray against *A. gambiae*, and has shown that although this species is not deterred from entering treated habitations, nevertheless, having fed on human beings, it leaves the house without having taken up sufficient DDT to cause its death. HOCKING (*ibid.*, 879) concludes that in East Africa "*A. gambiae* and *A. funestus* tend to leave a lightly treated building, but that with an impregnation of about 200 mgm per square foot, final mosquito mortality approaching 100 per cent will be achieved, and that on most surfaces the effect will last for at least 4-6 months unless lime is present."

It would appear from these statements, therefore, that in the case of the American vector *A. quadrimaculatus* and of the African vector *A. gambiae*, control by residual DDT spraying will not be fully efficient unless it results in the deposit of not less than 200 mgm DDT per square foot.]

R M Gordon

LINK, V B A Preliminary Report on Malaria Control by DDT Residual Spraying *J National Malaria Soc* 1947, June, v 6, No 2, 124-30, 5 figs

It is estimated that during the war over half a million U S troops contracted malaria. A certain unknown proportion of these men have now returned as carriers, and have thereby increased the malaria risk to the rest of the population. So far, there has been no evidence of any interruption of the downward trend of reported cases of indigenous malaria, but in order to combat the possible transmission of malaria from returning Service men, an energetic programme directed primarily against the adult mosquitoes [see BRADLEY & FRITZ, above] has been initiated by the U S Public Health Service and named the "Extended Malaria Control Program" to distinguish it from the "Malaria Control in War Areas Program". The latter programme, which was carried on during the war, had the opposite object, *i.e.*, to protect troops in the United States from acquiring malaria from the civilian population. The author is careful to point out that the effect of the extended programme in accelerating the downward trend of malaria in the U S A is difficult to measure, since the decrease was observed long before the introduction of DDT. The present paper deals with two surveys, one in South Carolina and the other in Porto Rico, in which the author estimated the residual effect of spraying with DDT on the parasite rates in the human population.

(1) *South Carolina* An area adjacent to the Santee Cooper Reservoir was selected. This region was chosen because it represented the "only known high endemic malaria area in the United States. Nearly 20 per cent of the population showed positive blood films in October 1944". A portion of the area adjacent to the reservoir was divided into approximately two equal parts, each having a population of about 1,500 people of whom 90 per cent were negroes. One of the areas was used as a control and the other sprayed with DDT. Before the spraying blood surveys were conducted in October 1944, and in April 1945, while the spraying was carried out in the last two weeks of April 1945 and again during the last two weeks of July 1945. Post-spraying surveys were carried out at monthly intervals beginning in June 1945, and are still being continued. The results of these surveys show that the malaria prevalence in

the unsprayed area rose during the transmission season, but remained at a stationary level in the sprayed area. Apparently no examination was made of the insect vector which in this region is *Anopheles quadrimaculatus*.

(2) *Porto Rico*. Two villages, selected as comparable, were used in this experiment one village being left untreated, while the other was sprayed in November 1944 July 1945 and again in November 1945. Three blood film surveys were made the first in the late autumn of 1944 the second in the spring of 1945 and the third in the late autumn of the same year. The results of these surveys are shown in the following table —

*Per cent. positive blood slides by age groups, Porto Rico November 1944 to November 1945*

Survey	Humacao Playa (Sprayed)								
	Under 10			Over 10			Total		
	Slides	Pos.	Per cent.	Slides	Pos.	Per cent.	Slides	Pos.	Per cent.
November 1944	483	28	5.8	977	57	5.8	1,460	85	5.8
March, 1945	440	15	3.4	782	19	2.3	1,202	34	2.8
November 1945	406	1	0.2	687	9	1.3	1,093	10	0.9

Survey	Loiza Aldea (Unsprayed)								
	Under 10			Over 10			Total		
	Slides	Pos.	Per cent.	Slides	Pos.	Per cent.	Slides	Pos.	Per cent.
November 1944	380	21	5.5	891	39	4.4	1,271	60	4.7
March, 1945	276	5	1.6	576	8	1.4	852	13	1.5
November 1945	282	6	2.0	576	27	4.7	858	33	3.8

Courtesy of Sanitary Engineer (R) Porter Stephens, C.D.C. District Representative, San Juan, Porto Rico.

The vector of malaria in Porto Rico is *Anopheles albimanus* which seldom remains within houses except for a few hours during the night. Animal bait traps and light traps, which were used for making collections throughout the year showed that *Anopheles albimanus* was present in sufficient numbers during the study period to transmit malaria, from one to several hundred of these species being collected from all traps during each night. From the results obtained from these two surveys, the author concludes that spraying of homes with DDT decreases the incidence of human malaria.

[In view of the similarly satisfactory results recorded by Bradley and Fritz also members of the Communicable Disease Center when using DDT at a concentration of 200 mgm. per square foot, and basing their conclusions on changes observed in the *A. quadrimaculatus* population it is unfortunate that the author of the present paper has omitted to mention the concentration or method of application of the residual DDT spray responsible for reducing the malaria incidence in the human population. Such information would be particularly interesting in the case of *A. albimanus* whose short indoor resting period presumably reduces its chances of acquiring a lethal dose of DDT.]

R. M. Gordon



BANG, F B, HAIRSTON, N G, MAIER, J & ROBERTS, F H S **DDT Spraying Inside Houses as a means of Malaria Control in New Guinea** *Trans Roy Soc Trop Med & Hyg* 1947, July, v 40, No 6 809-22, 2 charts

This paper describes the reduction in malaria transmission as a result of spraying houses with DDT in a native village, Motu Motu, on the southern coast of Papua, 150 miles west of Port Moresby. A comparable village two miles away was observed as a control. The villages are on swampy land, which is an excellent breeding ground for *A punctulatus moluccensis* [*A punctulatus farauti*] and *A subpictus*. The thatch houses are built on piles 6 to 8 feet above ground. The floors are of rough-hewn planks, laid loosely together, the walls are of woven palm leaf, thatch, or bamboo strips. Adult anophelines may be taken in numbers underneath the houses throughout the night. Though malaria is hyperendemic, mosquito infection rates were very low, anopheline prevalence was, however, extremely high.

All the 126 houses in the experimental village were sprayed in two days. Only the interior of houses was treated, walls, partitions, and the adjoining edge of floor and roof. If the walls were very low, part of the roof was also sprayed. A 4 per cent solution of DDT in kerosene was used at a rate of 100 mgm of DDT per square foot. Four months later, the number of *A punctulatus moluccensis* and *A subpictus* was less than 5 per cent of that found in neighbouring villages. In the control untreated village, there was an increase in both parasite and spleen indexes. In the treated village, the spleen index remained the same and the parasite index was slightly decreased. There was no change in the amount of *P falciparum* infection or of the parasite density in positive smears.

*A subpictus* was found infected in nature. [It is an important vector in Celebes]

Norman White

JOHNSON, H A & GOODMAN, W L **DDT in Oil as a Mosquito Larvicide** *Pub Health Rep* Wash 1947, Aug 15, v 62, No 33, 1191-8

Oiling to destroy mosquito larvae requires the application of 15 to 30 gallons per acre. Incorporation of DDT very substantially reduces the amount to be applied, and the difficulties of labour and transport. Field experiments in Arkansas were conducted in 1944 and 1946 to explore the new method. The DDT solution in kerosene was applied by means of a hand-atomizer by an operator walking at one or two constant speeds to give between 1 and 3 gallons per acre. A proprietary spreading agent was added at the rate of 0.5 per cent. Results were estimated on dipping counts before and twenty-four hours after treatment. It was observed that, with concentrations of DDT between 0.3 and 1.25, satisfactory kills of larvae of *A quadrimaculatus* were obtained when about 75 gm of DDT were applied per acre. Partial kills were obtained with 50 gm per acre and below.

J R Busvine

SAUTET, J, AUDOUIN, A, LEVAVASSEUR, G & VUILLET, Jeanne, Mlle **Action sur les larves de moustique, d'une suspension pure de DDT obtenue par les ultrasons** [**Action on Mosquito Larvae of Pure Suspensions of DDT obtained by Treatment with Supersonic Waves**] *C R Acad Sci* 1947, Jan 6, v 224, No 1, 66-7

The use of DDT against mosquito larvae has proved valuable, but the solvents or emulsions used in application are commonly harmful to other aquatic life. Fine suspensions are difficult to produce, but the following method is satisfactory. The DDT is dissolved in benzene, and water is added to it. Then the mixture is treated with supersonic waves (by an apparatus described

the unsprayed area rose during the transmission season but remained at a stationary level in the sprayed area. Apparently no examination was made of the insect vector which in this region is *Anopheles quadrimaculatus*.

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November 1944	483	28	5.8	977	57	5.8	1,460	85	5.8
March, 1945	440	15	3.4	782	19	2.5	1,202	34	2.8
November 1945	406	1	0.2	687	9	1.3	1,093	10	0.9

Survey	Loiza Aldea (Unsprayed)								
	Under 10			Over 10			Total		
	Slides	Pos.	Per cent.	Slides	Pos.	Per cent.	Slides	Pos.	Per cent.
November 1944	380	21	5.5	801	39	4.4	1,271	60	4.7
March, 1945	276	8	1.8	576	8	1.4	852	13	1.5
November 1945	282	6	2.0	576	27	4.7	858	33	3.8

\*Courtesy of Sanitary Engineer (R) Porter Stephens, C.D.C. District Representative San Juan, Porto Rico.

The vector of malaria in Porto Rico is *Anopheles albimanus* which seldom remains within homes except for a few hours during the night. Animal bait traps and light traps which were used for making collections throughout the year showed that *Anopheles albimanus* was present in sufficient numbers during the study period to transmit malaria, from one to several hundred of these species being collected from all traps during each night. From the results obtained from these two surveys, the author concludes that spraying of homes with DDT decreases the incidence of human malaria.

[In view of the similarly satisfactory results recorded by Bradley and Fritz also members of the Communicable Disease Center when using DDT at a concentration of 200 mgm. per square foot, and basing their conclusions on changes observed in the *A. quadrimaculatus* population it is unfortunate that the author of the present paper has omitted to mention the concentration or method of application of the residual DDT spray responsible for reducing the malaria incidence in the human population. Such information would be particularly interesting in the case of *A. albimanus* whose short indoor resting period presumably reduces its chances of acquiring a lethal dose of DDT.]

R M Gordon

BANG, F B, HAIRSTON, N G, MAIER, J & ROBERTS, F H S **DDT Spraying Inside Houses as a means of Malaria Control in New Guinea** *Trans Roy Soc Trop Med & Hyg* 1947, July, v 40, No 6, 809-22, 2 charts

This paper describes the reduction in malaria transmission as a result of spraying houses with DDT in a native village, Motu Motu, on the southern coast of Papua, 150 miles west of Port Moresby. A comparable village two miles away was observed as a control. The villages are on swampy land, which is an excellent breeding ground for *A punctulatus moluccensis* [*A punctulatus farauti*] and *A subpictus*. The thatch houses are built on piles 6 to 8 feet above ground. The floors are of rough-hewn planks, laid loosely together, the walls are of woven palm leaf, thatch, or bamboo strips. Adult anophelines may be taken in numbers underneath the houses throughout the night. Though malaria is hyperendemic, mosquito infection rates were very low, anopheline prevalence was, however, extremely high.

All the 126 houses in the experimental village were sprayed in two days. Only the interior of houses was treated, walls, partitions, and the adjoining edge of floor and roof. If the walls were very low, part of the roof was also sprayed. A 4 per cent solution of DDT in kerosene was used at a rate of 100 mgm of DDT per square foot. Four months later, the number of *A punctulatus moluccensis* and *A subpictus* was less than 5 per cent of that found in neighbouring villages. In the control untreated village, there was an increase in both parasite and spleen indexes. In the treated village, the spleen index remained the same and the parasite index was slightly decreased. There was no change in the amount of *P falciparum* infection or of the parasite density in positive smears.

*A subpictus* was found infected in nature. [It is an important vector in Celebes.]

Norman White

JOHNSON, H A & GOODMAN, W L **DDT in Oil as a Mosquito Larvicide** *Pub Health Rep* Wash 1947, Aug 15, v 62, No 33, 1191-8

Oiling to destroy mosquito larvae requires the application of 15 to 30 gallons per acre. Incorporation of DDT very substantially reduces the amount to be applied, and the difficulties of labour and transport. Field experiments in Arkansas were conducted in 1944 and 1946 to explore the new method. The DDT solution in kerosene was applied by means of a hand-atomizer by an operator walking at one or two constant speeds to give between 1 and 3 gallons per acre. A proprietary spreading agent was added at the rate of 0.5 per cent. Results were estimated on dipping counts before and twenty-four hours after treatment. It was observed that, with concentrations of DDT between 0.3 and 1.25, satisfactory kills of larvae of *A quadrimaculatus* were obtained when about 75 gm of DDT were applied per acre. Partial kills were obtained with 50 gm per acre and below.

J R Busvine

SAUTET, J, AUDOUIN, A, LEVAVASSEUR, G & VUILLET, Jeanine, Mlle **Action sur les larves de moustique, d'une suspension pure de DDT obtenue par les ultrasons [Action on Mosquito Larvae of Pure Suspensions of DDT obtained by Treatment with Supersonic Waves]** *C R Acad Sci* 1947, Jan 6, v 224, No 1, 66-7

The use of DDT against mosquito larvae has proved valuable, but the solvents or emulsions used in application are commonly harmful to other aquatic life. Fine suspensions are difficult to produce, but the following method is satisfactory. The DDT is dissolved in benzene, and water is added to it. Then the mixture is treated with supersonic waves (by an apparatus described

in *C. R. Soc. Biol.*, 1946, v 140 641) which treatment drives off the benzene and leaves DDT in a very fine suspension. This suspension was lethal to *Galer praeus* down to one part in ten million within twenty four hours and nearly as effective towards *Theobaldia longicollis*. Such suspensions in practice would be unaffected by wind or rain.

J. R. BURTON

TARTWELL, C. M. ERICKSON, A. G. BISHOP, E. L. Effects of DDT Mosquito Larviciding on WBDNA. Part I. The Effects on Surface Organisms of the Routine Hand Application of DDT Larvicide for Mosquito Control [TARTWELL]. *Pub. Health Rep. Wash.* 1947 Apr 11 v 62, No. 15 525-54 9 figs. (3 on 2 pls.) Part II. Effects of Routine Airplane Larviciding on Bird and Mammal Populations [ERICKSON] *Ibid.*, Aug. 29 No. 35 1254-62, 4 figs. Part III. The Effects on the Plankton Population of Routine Larviciding with DDT [BISHOP] *Ibid.* 1963-8, 7 figs. (3 on 1 pl.)

These papers are the interim reports of a study undertaken by the U. S. Public Health Service in 1944. Section I represents the first year's work, and Sections II and III that of the second year. There will be a later year's study mainly on the effects on fish.

I. Quantitative sampling of the surface forms, and counts of the surface forms and of dead organisms on the water surface twenty-four hours after treatment, were the methods used for determining the effects of routine treatment with DDT larvicide.

In general, insects were by far the most sensitive organisms. Applications of 0.1 lb. per acre had a fairly substantial effect if repeated as a routine, especially on such large insects as *Dytiscidae*, *Gyrinidae*, *Hydrophilidae* and *Corixidae*. Even applications of 0.05 and 0.025 lb. per acre had some noticeable effect if they were repeated regularly though none of these rates had any pronounced detrimental action in a single application. DDT dust treatments were less severe than DDT-foot-oil solutions.

The seasonal effects of routine DDT treatments, as indicated by a comparison of the populations of surface organisms in treated and untreated ponds, were marked. There was an increase in numbers of *Oligochaeta*, *Nematoda* and *Copepoda* and a decrease in insects, especially *Chironomidae*. Although the forms which increased were very numerous it is unlikely that they compensated in bulk or suitability as fish foods for the decrease in insects.

The direct effect on fishes was early observed to be detrimental at rates of 0.4 lb. per acre or more. Routine treatments at 0.1 lb. per acre caused some fish mortality after 3 to 10 treatments. It would appear to be unsafe to use routine treatments of DDT above 0.05 lb. per acre. This rate is safe except for shallow waters treated, all over repeatedly.

II. The effects of routine (weekly) applications of DDT sprays by aeroplane were observed in 1945 and 1946 at Savannah River Refuge, South Carolina. The DDT larvicide was applied as a thermal aerosol over two large ponds, and as a spray over two more. Observations on ten islands and six dykes were made on the numbers of birds and mammals found active throughout the season.

The results indicated no significant effects in the numbers of birds, cotton rats, house mice, rabbits or raccoons.

III. A special plankton trap and a plankton pump were used to determine the effects of hand applications of DDT larvicide to floating organisms in ponds. The DDT was applied at rates between 0.2 and 0.05 lb. per acre.

The results showed that the effects of DDT were relatively small compared with the variations due to climatic and other ecological factors, and not likely to be important.

J. R. BURTON

KIKUTH, W & MUDROW, Lilly Frühstadien der Vogelmalariaparasiten nach  
Sporozoiteneinfektion [Early Stages of Bird Malaria Parasites after  
Sporozoite Infection] *Klin Woch* 1939, Nov 11, v 18, No 45, 1443-4,  
2 figs

In this note, the authors discuss the origin of exoerythrocytic schizonts in bird malaria and point out that up to the time of writing the paper under review there has always existed the possibility that they may have originated from erythrocytic pigmented forms. They now note that in experiments with *Plasmodium calhemerium* the injection of sporozoites into the pectoral muscle was followed by the appearance of a number of uninuclear exoerythrocytic forms and a red nucleus. In addition to these uninuclear forms, two more advanced stages with 2 and 3 nuclei were found. Examination of a bird killed 24 hours after inoculation was negative, but a single uninucleated parasite was found in one killed 40 hours after inoculation. The authors consider that these observations prove that the sporozoite actually develops into non-pigmented exoerythrocytic forms. [This paper, published in 1939, has only recently been received.]  
C M Wenyon

PARAENSE, W L Ação patológica das formas exoeritrocitárias do *Plasmodium gallinaceum* 1 Investigações preliminares 2 Prova terapêutica da ação patológica 1 [Pathogenic Action of Exoerythrocytic Forms of *Plasmodium gallinaceum* 1 Preliminary Investigations 2 Therapeutic Test of Pathogenic Action] *Mem Inst Oswaldo Cruz* 1946, v 44, No 1, 147-92, 7 figs, 6 graphs & 4 pls (3 coloured) [21 refs] English summary

When young chicks were inoculated with sporozoites of *Plasmodium gallinaceum* exo-schizonts appeared before erythrocytic forms, since the former are products of sporozoite division. When parasitized blood was inoculated, the first forms to appear were erythrocytic forms. If quinine treatment was given to the chicks following blood inoculation, the chicks died between the 14th and 17th days when it was found that the brain was teeming with exo-schizonts. On the other hand, the blood infection could not be suppressed, as young trophozoites were always present. The control chicks untreated by quinine all died before the 8th day. In another experiment, 80 5-day-old chicks were each inoculated intravenously with 65,000 000 parasites. Death occurred in the untreated controls in 4 to 6 days while in the treated group death occurred in 10-15 days. Exo-forms were present in the brain of the treated group but not in the controls, which showed a massive blood infection. Trophozoites were present in the blood of the treated chicks and these increased in number from the 7th day till the time of death, when there were present about 20 per 100 erythrocytes. When the dose of parasites injected was less than 2,800 per bird, all but two of the treated birds died between the 18th and 21st days. Of untreated birds, two died at the peak of the blood infection and neither showed any exo-infection in the brain. The remaining untreated birds survived this period and died between 21st and 24th days with heavy exo-infection of the brain. It seems evident that the resistance to acute infection in untreated birds was equivalent to the action of quinine in treated birds. In a batch of quinine-treated chicks, examination of the blood and of brain tissue obtained by biopsy was carried out with the object of determining any relationship which might exist between the blood parasites and exo-forms in the brain. The two curves showed a striking parallelism, so that it appears that the increasing trophozoites in the blood of quinine-treated chicks is a direct result of the exo-forms in the brain. In two chicks, recrudescence of parasites occurred 20 days after the beginning of latency. In these chicks there was the

same parallelism between the number of blood trophozoites and exo-forms in the brain. The lack of schizogonic development of the blood trophozoites, beyond suggesting parasitocidal antibodies, appears to indicate that malarial immunity is stimulated by erythrocytic parasites alone as the exo-forms were completing their normal development. In all these experiments, it was not possible to eliminate the blood infection and it remains to be proved whether death is due to the blood form or to the exo-stages in the brain.

An attempt was made to eliminate the blood infection by use of sulphadiazine. Ten 5-day-old chicks were inoculated intravenously and given quinine from the 3rd day. On the 8th day sulphadiazine (1.0 mgm. per kilo of body weight) was given twice daily to 4 of the birds in addition to the quinine. All the quinine-treated birds died between the 14th and 17th days and showed the usual increase of blood trophozoites. The 4 chicks treated with sulphadiazine were examined by brain biopsy on the 4th, 7th and 8th days of treatment. In the brain of all were found damaged exo-forms, while blood smears were negative though the presence of a subpatent infection was demonstrated by blood inoculation to healthy chicks. When treatment was suspended, the blood forms increased and all the birds died with heavy exo-infections. In another experiment, the sulphadiazine was given on two or three occasions with the result that there was a greater survival of the birds treated with sulphadiazine and quinine. The finding of altered exo-forms in the surviving birds is an indication of the rôle the exo-forms play in the death mechanism.

C. M. HAYSON

WILLIAMSON J & LOURIE E. M. Acquired Paludrine-Resistance in *Plasmodium gallinaceum*. I. Development of Resistance to Paludrine and Failure to develop Resistance to certain other Antimalarials. *Ann. Trop. Med. & Parasit.* 1947 Sept. v 41 No. 2, 278-91 [30 refs.]

It was recently shown by BISHOP & BIRKETT and by the present authors [this *Bulletin* 1947 v 44 989-970] that resistance to paludrine which persisted after passage in *Aedes* mosquitoes, could be produced in *P. gallinaceum*. The same strain could not be made resistant to mepacrine, quinine, M 3349 or sulphadiazine. The present paper gives further details of these experiments. With the four last-named drugs, chickens 8- to 9-weeks old were used as hosts and serial inoculation was carried out from one treated bird to another. If the birds survived the course, six daily drug treatments per week were given for two weeks after parasites had been detected in the blood. The survivors, except in the case of those which received sulphadiazine, were generally heavily infected with exoerythrocytic forms. After  $\frac{1}{2}$  years of treatment drug-resistance was not detected.

Six-days-old chicks were used as hosts in the production of a paludrine-strain. One series of birds was treated with the minimum effective drug for the normal strain and a second series with the maximum dose by the host. Treatment was started on the day of intravenous inoculation with parasitized red cells and was then continued twice daily for 3 days. In the first series, resistance was established after about 3 months and quit suddenly in the second series it appeared at approximately the same time as a result, it is believed, of mutation. About 20-40 times as much drug was tolerated by the resistant strains of parasites as by the normal without apparent change in morphology. The resistance to paludrine did not extend to other drugs, except the  $N_6$ -methyl derivative. The possible mechanism of production of drug resistance and its significance in the treatment of human malaria with this drug are discussed.

J. D. FULLON

**MARSHALL, P B** Mode of Action of "Paludrine" [Correspondence] *Nature*  
1947, Oct 4, 463

HAWKING [this *Bulletin*, 1947, v 44, 648] has given evidence that paludrine is inactive against malarial parasites *in vitro*, but becomes active after it has undergone some metabolic change in the body. In contrast, Marshall finds that paludrine 1/60,000 produces a greater inhibition of oxygen consumption of *P. gallinaceum* in the presence of glucose or lactate than does quinine 1/6,000. Inhibition of oxygen consumption by paludrine is essentially different from that by iodo-acetic acid. The author suggests that paludrine exerts its anti-malarial action, at least partially, by inhibiting the oxidation processes of the malaria parasite, but not the anaerobic breakdown of glucose to lactic acid. However, the concentrations required to produce these effects are higher than those occurring in therapy or those used by Hawking, so their significance is not yet certain.

F Hawking

**RIGDON, R H** An in Vitro Study of the Mechanism producing Rapid Diminution in the Parasitemia in Ducks infected with *Plasmodium lophurae* *Amer J Hyg* 1947, Sept, v 46, No 2, 254-9, 3 figs

Oxygen, nitrogen, and carbon dioxide are bubbled for two hours through citrated blood obtained from ducks infected with *P. lophurae*. The blood is then inoculated into clean ducklings and the degree of parasitaemia is measured in the ensuing infections, the results being compared with an injection of untreated blood as a control. Treatment with carbon dioxide resulted in a lesser degree of parasitaemia than did that with nitrogen or oxygen. The author suggests that the accumulation of CO<sub>2</sub> in the body at the peak of the infection may be the cause of the sudden drop in numbers of parasites following the crisis.

[So many different factors are involved that it is difficult to conclude much from these experiments. The author states in the discussion that one should be careful in assuming that CO<sub>2</sub> is lethal for the plasmodia, and yet in the summary says that "apparently the plasmodia are killed by the CO<sub>2</sub>"]

P C C Garnham

**THOMSON, K J, FREUND, J, SOMMER Harriet E & WALTER, Annabel W** Immunization of Ducks against Malaria by means of Killed Parasites with or without Adjuvants *Amer J Trop Med* 1947, Mar, v 27, No 2, 79-105, 15 figs & 1 pl

In a previous paper, the authors have referred to experiments showing that it is possible to immunize ducks against *Plasmodium lophurae* with a vaccine consisting of formalin-killed parasites combined with paraffin oil containing killed tubercle bacilli and an emulsifying agent [this *Bulletin*, 1946, v 43, 311]. In the present paper further details are given. It is possible to immunize adult ducks against infection with *P. lophurae* and *P. cathemerium* by injection of the vaccine. With *P. lophurae* immunity is revealed by prevention of death or by lowering the degree or shortening the duration of parasitaemia and with *P. cathemerium* by modifying the course of parasitaemia. Repeated intramuscular injections protect adult ducks for six months, but single injections with multiple sites protect to a less extent. If the injections are given into the subcutaneous fat and not into the muscle no protection results. In ducks, the inclusion of killed tubercle bacilli in the vaccine gave rise to amyloidosis of the liver and spleen, but this did not influence the immunity in any way. In monkeys immunized against *P. knowlesi* by vaccine containing killed tubercle bacilli amyloidosis did not occur.

C M Wenyon

RIVERO M. D. La infección experimental por el *Haemoproteus columbae* Celli y Sanfelice. [Experimental Infection with *H. columbae*.] *Medicina*. Mexico. 1947 May 10 v 27 No. 531 197 204 9 figs.

Two views exist as to the method of transmission of *Haemoproteus columbae* from pigeon to pigeon. According to ARACIO species of *Lychnis* infect themselves by taking up blood from an infected bird. In the intestine, flagellation of the male gametocyte occurs and the fertilized female becomes an ookinete. This discards its pigment and as such is inoculated to the pigeon. According to ADIE the ookinete in the intestine of the *Lychnis* penetrates the wall of the stomach and develops into an oöcyst, giving rise to sporozoites which invade the salivary glands.

In order to test these views, the author has followed the development of the parasite in larvae of *Triatoma*. This proceeds as far as the formation of ookinetes but no further. With the contents of the stomach of triatomas 4-48 and 72 hours after feeding on an infected pigeon, uninfected pigeons were inoculated intravenously. From the 12th to the 20th days after the inoculation the blood showed invasion by young gametocytes which during the following two months developed into mature forms. It is evident that the ookinetes are able to start an infection as ARACIO had maintained. [See also this *Bulletin* 1941 v 33, 568.]

C. M. Newson

## TRYPANOSOMIASIS

FAIRBAIRN H. The Infection of Rats by *Trypanosoma* (*T. rhodesense*) taken from Man early in the Disease. *Ann. Trop. Med. & Parasit.* 1947 Sept. v 41 No. 2 218-25 1 fig.

In this work the author has continued to study the relation between the electric charge carried by trypanosomes and the results obtained in experimental trypanosomiasis [see this *Bulletin* 1947 44 649]. A single strain of *Trypanosoma rhodesense* (isolated in 1934 from a human case) was used, but "lines" of the strain had been maintained in sheep, Thomson's gazelle, and monkey by cyclical transmission through *Glossina* *swetschikovi*.

Tsetse flies infected with one or other of these "lines" were allowed to bite human volunteers. Fluid from the site of the bite was examined daily and, when trypanosomes first appeared, blood from that site was used to inoculate rats and to prepare films for studying the morphology of the trypanosomes. In the same way when trypanosomes showed in ordinary blood films venous blood was taken for blood films and for rat inoculations.

Four types of results were obtained in the rat experiments. In Group I all rats became infected after the usual incubation period of 4-8 days. In Group II all rats became infected after an increased period of incubation (9-18 days). In Group III some rats were infected after incubation periods varying from 8-50 days and others remained uninfected. In Group IV all rats remained healthy.

The length distributions of the 6 types of trypanosome recognized by the author (long, intermediate, short, each either positively or negatively charged) were determined from the blood films. All types were present in each group though in different proportions, but only the long type need be considered. By the author's hypothesis the other types cannot initiate infection for which both the positively and negatively charged forms of the long type are required. From previous observations, the normal mean length for the positive form of *T. rhodesense* is 29 $\mu$  and for the negative form 28 $\mu$ . In Group I a considerable



proportion of individuals had lengths greater than the general mean in Groups II, III and IV the proportion was progressively less. Relating this finding to the result of the rat experiments, the author suggests that trypanosomes whose length is above the mean are "mature". They alone can enter into syngamy and produce infection. [The author and his co-worker CULWICK are putting forward new concepts on trypanosomiasis, so it is their duty to plan their experiments in such a manner that the results provide unequivocal evidence for or against their hypothesis. The experiments detailed in this communication fail, in the reviewer's opinion, to achieve this end. Why is it important to test the virulence to rats of the trypanosomes on their first appearance in the blood? No reason is advanced. No consideration is given to the author's discussion of his results to an apparent relation between the 'line' of the trypanosome and its virulence to rats. For instance, Table I shows that of 144 sheep-line-man-rat tests 65 (95 per cent) were positive, whereas of 69 monkey-line-man-rat tests 51 (35 per cent) were positive. The fact is noted that no comment is made. Then when dealing with syngamy of the long forms, the statement is made that the argument does not apply to syringe-passage strains which consist only of long forms, although their mean length is reduced. Inoculation of a single trypanosome of these strains will produce infection, and this is taken to mean that genetic segregation has taken place, since conjugation to produce short and intermediate forms cannot occur. Surely this is assuming the correctness of the hypothesis which the experiments are supposed to be testing.]

J C Broom

VANDERPLANK, F L. Experiments in the Hybridisation of Tsetse-Flies (*Glossina*, *Diptera*) and the possibility of a New Method of Control. With Appendix I by W H Porrs. *Trans Roy Entom Soc London* 1947, June 30, v 98, Pt 1, 1-18, 8 figs on 2 pls [12 refs]

The author writes about what would perhaps be better described as "cross-pairing" rather than "hybridisation" between two closely related species of tsetse *G. morsitans* and *swynnertonii*.

The virgin female tsetse is attractive to the male very early in life and pairing takes place either before or very soon after the first meal. The author finds that if both sexes of these two species are kept together in a cage, mating female ceases to be attractive to the male for the rest of her life. The author is random that is to say, the number of matings with an individual of the same and of the other species is determined by abundance, and there is no "preference" for a partner of the same species.

When pairing takes place, either with a male of the same or of the opposite species, the female is generally, though not always, inseminated. If the pairing has been with a male of the other species she is in effect sterilized, for she ovulates in a normal way but the eggs fail to hatch as a somewhat rare event. The egg will hatch and eventually give rise to a normal pupa. The hybrid that emerges from such a pupa resembles *G. swynnertonii* in its external characters whichever species may have supplied the mother. In the case of a male hybrid, it is found that the genitalia exhibit intermediate characters, no similar differences can be shown in females which are in any event indistinguishable in these closely related species. The hybrids are themselves sterile.

The author shows that in nature the two species overlap in certain areas, in which a few males with intermediate genitalia occur. As such individuals are never found except where the two species are present, one is justified in regarding them as hybrids. He also shows that if large numbers of *morsitans* are introduced into an area inhabited solely by *swynnertonii* cross-pairing

RIVERO M. D. La infección experimental por el *Haemoproteus columbae* Celli y Sanfelen. [Experimental Infection with *B. columbae*.] *Medicina*. Mexico. 1947 May 10 v 27 No. 531 197-204 9 figs.

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C. M. JENYON

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J C Broom

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The author writes about what would perhaps be better described as "cross-pairing" rather than "hybridisation" between two closely related species of tsetse *G. morsitans* and *swynnertoni*.

The virgin female tsetse is attractive to the male very early in life and pairing takes place either before or very soon after the first meal. After pairing the female ceases to be attractive to the male for the rest of her life. The author finds that if both sexes of these two species are kept together in a cage, mating is random—that is to say, the number of matings with an individual of the same and of the other species is determined by abundance, and there is no "preference" for a partner of the same species.

When pairing takes place, either with a male of the same or of the opposite species, the female is generally, though not always, inseminated. If the pairing has been with a male of the other species, she is in effect sterilized, for she ovulates in a normal way but the eggs fail to hatch—as a somewhat rare event the egg will hatch and eventually give rise to a normal pupa. The hybrid that emerges from such a pupa resembles *G. swynnertoni* in its external characters, whichever species may have supplied the mother. In the case of a male hybrid, it is found that the genitalia exhibit intermediate characters; no similar differences can be shown in females, which are in any event indistinguishable in these closely related species. The hybrids are themselves sterile.

The author shows that in nature the two species overlap in certain areas, in which a few males with intermediate genitalia occur. As such individuals are never found except where the two species are present, one is justified in regarding them as hybrids. He also shows that if large numbers of *morsitans* are introduced into an area inhabited solely by *swynnertoni* cross-pairing

occurs and occasional hybrids are produced. It is likely therefore on the basis of the laboratory work, that many other females have been inseminated by the male of the introduced species and are thereby sterilized (though this is not actually demonstrated). The method might perhaps be used to attack a species in nature, especially if the numbers have been brought to a very low level by some other method. The method could only be employed where the introduced species would be able to live in the environment in which it is liberated but could probably not occupy it permanently. P. A. Buxton

**NATURE, 1947 Oct. 11 485-6. D.D.T. and the Aeroplane in the Control of the Tsetse Fly and Trypanosomiasis in South Africa.**

The note describes a meeting in London in September 1947 at which Dr P. J. DU TOIT discussed recent South African work against tsetse and showed a film.

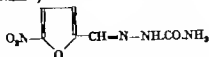
The particular problem was the control of *Glossina pallidipes* in a small game reserve in Zululand. In the most recent work, an attempt is made to control this insect by DDT smoke obtained by discharging a concentrated solution into the hot exhausts of aircraft, and sublimating the insecticide, which then falls and is found to penetrate dense bush. The smoke was put down by Anson aircraft flying cross wind at 120 m.p.h. the effective swath was 70 yards at wind speeds of about 6-10 m.p.h. At any one moment a large proportion of the tsetse population is in the pupal stage in the soil the smoke was therefore put down on six occasions over a period of weeks. The cost of insecticide for six occasions is given as 12s. per acre, and the cost of aircraft services as 6s. (which is surely a token figure).

In broken ground, with ravines, where low flying would be exceptionally difficult, DDT smoke may be produced by small generators placed by ground party.

The catches after spraying were exceedingly low but no figure is given. Harms traps have in years past also made an enormous reduction in the same insect in the same area, but never exterminated it. [The speaker was, it seems, rather optimistic: he hoped that a very great mortality having been produced, nature would step in and do the rest.] P. A. Buxton

- i. DODD M. C. The Chemotherapeutic Properties of 5-Nitro-2-Furaldehyde Semicarbazones (Furacins). Reprinted from *J. Pharm. & Exp. Therap.* 1946 Apr. v 86 No. 4 311-23. [10 refs.]
- ii. KRANTZ, J. C. Jr & EVANS W. E. Jr. A Contribution to the Pharmacology of 5-Nitro-2-Furaldehyde Semicarbazones. *Ibid.* 1945 Dec. v 85 No. 4 324-31 1 chart.

L It has been found that a nitro group in the 5-position confers definite antibacterial properties on a variety of 2-substituted derivatives of furane. The most promising of an extensive series examined was 5-nitro-2-furaldehyde semicarbazone ("Furacin") —



"Furacin" is active not only against a wide range of bacteria *in vitro* and *in vivo* but also against *Trypanosoma equiperdum* infections. Its activity against bacteria embraces both Gram-positive and Gram-negative organisms.

as well as *Mycobacterium tuberculosis*, but it is conspicuously without effect against *Ps. pyocyanea*, and is only very slightly active against *Str. viridans* and *Str. pneumoniae*.

The compound is only slightly soluble in water (1/4,200), and for therapeutic tests, carried out in mice and rats, it was administered as a suspension in 10 per cent gum acacia, by stomach tube, or in 10-20 per cent gum acacia subcutaneously or intravenously. Details are given of successful results in infections with two Gram-positive bacterial species (*Staph. aureus* and *Str. haemolyticus*) and two Gram-negative species (*Salmonella paratyphi B* and *Salmonella typhi-murium*).

There was a fairly high degree of activity against *T. equiperdum* infections, the following therapeutic indices being given, where treatment was by stomach tube—For mice LD50/CD50, 9. For rats, LD100/CD100, 8.

Histological examination of organs from animals sacrificed after oral treatment with maximal dosages failed to reveal the pathological basis for the drug's toxic action at high dosage-levels. However, maximal subcutaneous doses gave rise to severe hepatitis and extensive degeneration of the tubular epithelium of the kidney.

[There is an important gap in the data on this compound's performance against *T. equiperdum* infections. The tests against bacterial infections generally showed the curious feature that a dose of about 150 mgm per kgm orally produced the maximal therapeutic effect, whilst larger doses—though still well below the lethal range—gave significantly poorer results. For example, in *Staph. aureus* infections in mice survival-rates after dosages of 150, 200 and 250 mgm/kgm were 63.3, 36.7, and 40.0 per cent respectively, again, in *Salmonella paratyphi B* infections the rates were 58.3, 61.7 and 33.3 per cent respectively. Deaths after treatment by the highest dose were the result of infection and not of toxic action of the drug. In the protocols given for tests against *T. equiperdum* infections, however, no results are recorded for doses higher than 150 mgm/kgm for mice and 100 mgm/kgm for rats.]

Standard pharmacological and biochemical techniques were employed in order to determine the toxic potentialities of "Furacin". The observations included studies of the effects of the compound on blood pressure, respiration, and the heart-beat as shown by electrocardiogram and by direct observation during perfusion or after extirpation. The effects on cytochrome oxidase and tissue dehydrogenase activity were also studied. Acute and chronic toxicity tests in rats, mice and monkeys were supplemented by blood counts and histopathological studies on the organs of animals which had received the highest dosages.

These tests revealed a very low degree of toxicity. Several persons were given 100 mgm orally three times a day, without symptoms being produced. The dose was increased to 2-4 gm daily which resulted in nausea in 20 per cent of cases. There were no changes in the blood or urine of these persons [The numbers treated are not stated]. [See also *Bulletin of Hygiene*, 1946, v 21, 614.]

E. M. Lourie

PINTO C. Epidemiologia da doença de Carlos Chagas no Estado do Rio Grande do Sul—Brasil [Epidemiology of Chagas's Disease in the State of Rio Grande do Sul, Brazil]. *Mem. Inst. Oswaldo Cruz* 1946, June, v 44, No 2, 363-400, 26 figs. (3 maps).

After briefly describing the physiographical features of the State, the author relates that Sanitation Posts have been established in 78 of the 92 municipal districts and that during the 8 years, 1939-46, 73 cases of Chagas's disease have been observed, the largest number in any single year was 27 in 1942. *Triatoma infestans* is the vector. *Eutritoma rubrovaria* is found in the burrows of the

armadillo *Dasypus hybridus* in the open fields during the winter in temperatures about zero Centigrade. Of the total cases 48 were in children (32 in adults in 3 the age was not known. Forty-seven were acute, of whom 36 were children, 7 adults, 2 not known and of 23 chronic cases (this makes a total of 72 only) 11 were children and 14 adults. As regards nationality 33 were whites, 4 negroes, 3 mulattoes, but as many as 28 were not known. In all the acute cases Romana's sign was present and in 13 there was some cardiac disturbance—tachycardia, arrhythmia, extra-systoles or signs of myocarditis. Diagnosis was made either by direct blood examination or by xenodiagnostic methods. Details as to nationality, age, sex, clinical characters, etc. are given for each patient in a table. The houses were infested with *Triatoma* and these were often found collected under the mattresses in the cold weather.

The article contains several maps of the district, photographs of the country and meteorological and epidemiological details in graphs.

H. Harold Scott

MAYER, M., PIZANO C., F. & MEDINA, R. Aspectos epidemiológicos de la enfermedad de Chagas en Venezuela. Bases para una campaña de saneamiento aplicable a zonas endémicas del medio rural Venezolano. [Epidemiological Aspects of Chagas Disease in Venezuela.] *XII Conferencia Semestral P. n. americana. Cuadernos Amarillos. Publicaciones de la Comisión Organizadora* A 20 Caracas, 1946 68 pp. 1 map.

MUNIZ, J. Do valor da reação de precipitina no diagnóstico das formas agudas e sub-agudas da Doença de Chagas ("Trypanosomiasis Americana") [A Precipitin Reaction in Diagnosis of Acute and Subacute Forms of Chagas's Disease.] *Brasil-Médico*, 1947 July 19 & 28 v. 61 Nos. 29/30 281-7 1 graph & 1 fig. English summary

The author with his colleague DE FREITAS, has previously published articles dealing with immunity reactions in Chagas's disease (see this *Bulletin* 1945 v. 42 875 1947 v. 44 571) complement fixation and agglutination. In the present paper he describes a precipitin reaction. The method of obtaining the extract is very detailed and those interested must consult the original—suffice it here to say that, by employing Fuller's method, he obtained from cultures of *T. cruzi* a stable, water-soluble fraction. A very small quantity of serum is needed and the results seem, in the author's hands at least to be very satisfactory. 0.1 cc. of serum (which must be quite clear and free from blood) of the suspected patient is placed in a small tube of 3 mm. diameter—an equal quantity of precipitinogen is added down the wall of the tube to form a layer over the serum. A control with physiological saline is put up at the same time. The tubes are left at room temperature. In strongly positive cases a disk appears at the surface of contact in 1-2 minutes (4 plus); less acute cases give the reaction in 10-20 minutes (3 plus) or even longer after half an hour (2 plus). In a table are given details of 21 cases, stating the length of interval since infection occurred, the results of the precipitin test and the agglutinating titre of the serum. The ages of the patients ranged between 7 months and 14 years. In most, the tests were made more than once at intervals up to 178 days after the date of infection. Adding these cases of acute disease to 12 previously noted the author states that in every one of the 33 the reaction was positive in the early weeks of infection and remained so for periods up to 4 months. The test is, therefore, of special value in the early stage before definite symptoms appear and takes less time than search for trypanosomes in the blood, and a positive result is not given by leishmaniasis patients (though immune sera prepared against leishmanial diseases do react). The reaction is of some quantitative value because it occurs as a rule when the agglutination

titre is 1 500 or over It has little value in chronic cases, only 18 per cent of more than 200 such patients gave a positive For these chronic cases, other methods, such as complement fixation or xenodiagnosis, are better

H Harold Scott

MUNIZ, J, NOBREGA, G & DA CUNHA, M Ensaio de vacinação preventiva e curativa nas infecções pelo *Schizotrypanum cruzi* [Attempts to vaccinate against *T cruzi* Infections] *Mem Inst Oswaldo Cruz* 1946, Sept, v 44, No 3, 529-41 English summary

Though the results were on the whole negative, this investigation was one of interest It is known that inoculation of cultures of *T cruzi* into rabbits results in the formation of specific antibodies, their serum agglutinating in titres up to 1 50,000 The authors have utilized Rhesus monkeys, *Macaca mulatta*, because infection of *T cruzi* in them evolves very like that in man They tested the value of the vaccine (killed by merthiolate 1 10,000) prophylactically and curatively after infection, inoculation was made intradermally, subcutaneously, intramuscularly and intravenously The details are given minutely in a series of protocols and described in the text Those interested should study the original, suffice it here to repeat what has been said above that the vaccine proved neither protective nor curative in doses of 24-28 mgm

H Harold Scott

## LEISHMANIASIS

ROMAN, E Phlébotomes tunisiens de Tebourba et d'Ain-Draham [*Phlebotomus* from Tebourba and Ain-Draham, Tunisia] *Ann Parasit Humaine et Comparée* 1947, v 22, Nos 1/2, 68-74, 3 figs [13 refs]

A study of 543 *Phlebotomus* specimens in north Tunisia revealed the presence in Tebourba of *Phlebotomus minutus parroti*, *P perniciosus*, *P longicuspis*, *P perfiliewi* and *P papatasi* the first three species also occur at Ain-Draham Aberrant forms are described The possible local rôle of these species as vectors of leishmaniasis is discussed

H J O'D Burke-Gaffney

MACIEL, P & ROSENFELD, G Leishmaniose visceral Americana—Um caso de um novo foco [A Case from a New Focus of American Visceral Leishmaniasis] Reprinted from *Rev Clin São Paulo* 1947 May-June v 21, Nos 5/6, 51-61, 4 charts 1 fig & 1 map [36 refs]

DE BARROS, O M & ROSENFELD, G Leishmaniose visceral Americana Novo caso [A New Case of American Visceral Leishmaniasis] Reprinted from *Rev Clin São Paulo* 1944, v 15, No 4, 97-102, 5 figs (3 on 1 pl.)

KATZENELLENBOGEN, I Cutaneous Leishmaniasis in Palestine with a Report of a New Endemic Focus in the Negev *Harefuah*, Jerusalem 1947, Sept 14, v 33, No 6 [In Hebrew 98-100 (17 refs) English summary 100]

Revivim-Asluj, in the Negev, is a new Jewish settlement in Palestine with "sand-desert" conditions There are some 30 settlers there, and between September 1946 and January 1947, 25 of them developed oriental sores of a "dry" type after a residence of 1 to 2 years The sores also occur in nomad Bedouin in the neighbourhood of Revivim, but are absent in the case of settlers and nomad Arabs in other parts of the Negev

The salinity of the soil is high (0.25 to 1.0 per cent.) huge open reservoirs for rain water were built recently and there is a large cave in the settlement, which has been used as a "rest house" by nomads for centuries. Thus, conditions in Revivim favour the breeding of sandflies.

It is not considered that the spread of oriental sore in Palestine can be attributed to carriers from the Dead Sea area or from neighbouring countries, but it is presumed that latent foci of leishmaniasis-infected sandflies exist and that Revivim is one. Outbreaks of cutaneous leishmaniasis occur in Arabs and Jews alike when non-immune persons enter the area, as has already occurred in the Dead Sea.

H J O D Burke-Gaffary

PAVLOV P. Recherches sur la leishmaniose de chien. Dermobiose publication. [Studies in Canine Leishmaniasis. Second Report.] Bull. Soc. Path. Exot. 1947 v 40 Nos. 7/8, 238-43.

HAMPTON J W F. The Excretion of Stilbamidine and some related Compounds in Experimental Animals. *Ann. Trop. Med. & Parasit.* 1947 Sept., v 41 No. 2, 228-33. [10 refs.]

Studies on the excretion of stilbamidine by human subjects have previously been reported in this Bulletin [1943 v 40, 121 1945 v 42, 18] as well as similar investigations on laboratory animals (*ibid* 1946 v 43, 723). In the present paper the excretion of this substance and of a hydroxy amino- and iodo-derivative in the urine of rats and rabbits has been investigated after single or repeated doses. Stilbamidine itself was estimated by a modification of the fluorescent method of HARRIS & GRIMLEY (this Bulletin 1943 v 40 123) and also by the glyoxal method of FILLER (this Bulletin 1945 v 42, 234) after extraction of the bases from urine in butyl alcohol. Amino-stilbamidine was estimated by fluorimetric and diazotization procedures, iodo-stilbamidine colorimetrically and the hydroxy-derivative by the yellow colour of the base after its extraction by butyl alcohol other methods having proved unsuitable.

After a single intravenous injection of stilbamidine only about 1 per cent. of the administered dose was recovered in fluorescent form about twice this amount was recovered after repeated dosage. When the dose injected was small, excretion could not be detected till 5 doses had been given after 10 doses there was a sudden rise in the amount present in urine, suggesting that storage had been taking place in the body. The curious observation was made that "proportionately very much less of the compound was excreted by the animals receiving large doses than by those receiving small doses, when the reverse was expected."

The results of colorimetric estimation of stilbamidine indicated an excretion 20 times greater than that found by the fluorimetric method. In the case of amino-stilbamidine, higher results for excretion were obtained by the diazotization than by the fluorimetric method. Stilbamidine thus appears to be excreted largely in the form of a non-fluorescent (compound) the identity of which was not established. [When discussing the reason for the low excretion values found for stilbamidine by the fluorimetric method of estimation, the author incorrectly attributes to the reviewer the view that the addition of water occurs at the ethylenic linkage in stilbamidine when its solutions are exposed to light. Recently FULTON & DUNITZ (this Bulletin 1947 v 44 888, have shown by X-ray crystallographic methods that dimerization occurs with the formation of a cyclobutane derivative.)

J D Fulton



*Fevers of the Typhus Group*

THOMPSON, R H S & WHITTAKER, V P Antidotal Activity of British Anti-Lewisite against Compounds of Antimony, Gold and Mercury  
*Biochim J* 1947, v 41, No 3, 342-6, 1 fig [20 refs] [Summary appears also in *Bulletin of Hygiene*]

BAL protects the isolated pyruvate oxidase system of pigeon brain from poisoning by compounds of antimony, gold and mercury. Its antidotal potentialities *in vivo* may therefore be inferred. The compounds examined were — Antimony Tartar emetic, "Stibophen", and "Stibacetin". Gold Gold chloride, "Myocrisin", and 1, aurothioglucose. Mercury Mercuric chloride. [For other references to BAL in arsenical intoxication see *Bulletin of Hygiene*, 1946, v 21, 658, 737, 864, 1947, v 22, 189, 511] E M Lounie

## FEVERS OF THE TYPHUS GROUP

MACKENZIE, M Typhus Fever in England *Bull Office Internat d'Hyg Publique* 1946, Oct -Nov -Dec, v 38, Nos 10-11-12, 873-4 [French version 871-2]

Typhus fever is now rare in England and Wales, but during the war years special precautions against its importation became necessary. These included the provision of a panel of expert consultants, the selection of isolation hospitals as special centres, arrangements for disinfection of homes and contacts, the formation of special sanitary teams, provision of facilities for immunization of exposed medical and sanitary workers, the supplying of DDT and sprays to Local Authorities and the issue of a memorandum on louse-borne typhus fever.

Two types of yolk-sac vaccine were provided, one (Cox type) prepared by the U S Public Health Service and the other by the Connaught Laboratories, Toronto. Facilities were provided for the inoculation of authorized travellers abroad.

During the war, until 1944, only two suspected cases of typhus were reported in England and Wales. One was probably of the tick-borne type and therefore of no local epidemiological importance. The other was in a soldier who became ill a few days after an anti-typhus inoculation. In this case, the diagnosis was not confirmed as a result of serological tests.

The danger increased after the invasion of Germany and VE day, especially as regards the risk of infection being carried by returning prisoners of war. In fact, 21 such cases were imported, 14 in ex-prisoners of war and 7 in medical students returning from voluntary duty in Belsen. Measures taken to prevent secondary cases were successful and none occurred thereafter.

H J O'D Burke-Gaffney

BOYER, J Epidemiological Study of Cases of Typhus Fever found in the Paris Area on the Return of Prisoners and Deportees *Bull Office Internat d'Hyg Publique* 1946, Oct -Nov -Dec, v 38, Nos. 10-11-12, 865-70 [French version 855-64, 5 graphs]

Among prisoners and deportees who returned to France in 1945, there were 167 cases of typhus fever in Paris, which was the main centre for dealing with repatriated persons. There were only 15 secondary cases among persons who came in contact with the patients after their return to Paris. In four of the

secondary cases, the only contact had been with repatriated persons who had never suffered from fever and who, therefore, were assumed to have suffered from "inapparent" attacks of the disease.

Plans had already been made for prompt diagnosis of cases and for the disinfection and disinfection of all contacts, who were kept under close observation for 25 days instead of the 12-day period prescribed by international regulations. Contacts were not vaccinated because they ceased to incur risk of infection after detection, but nurses, doctors, and officials of the Repatriation Service were vaccinated with the Durand and Giroud vaccine. Only one vaccinated person was attacked, and she made a good recovery.

John W. D. Mearns

DIAS, A. de C. Typhus Fever in Portugal during the War Years. *Bull. Office Internat. d'Hyg. Publique*. 1948, Oct.-Nov.-Dec. v 38, Nos. 10-11-12, 878-80 [French version 875-7]

The influx of war refugees and the partial mobilization of Portuguese troops throughout the Portuguese empire exposed Portugal to a number of infectious diseases of these, typhus in particular was a serious risk, because of the great epidemic in Spain in 1941-42, which demanded stringent precautions along a wide stretch of the frontier. Indeed, of 50 cases which did occur in Portugal in 1941 more than half were traceable to the Spanish epidemic. It was proved that the disease was imported by gypsies, even in the city of Lisbon where typhus has always been rare.

Figures are given of incidence and deaths by ages, in Lisbon and the provinces, between which the cases and deaths were exactly evenly divided (25 and 3 in each respectively). It is noted that in Lisbon, none of the 3 deaths occurred in people over 50, when the severity is greater. In the provinces, 1 death occurred in a person over 50 and 2 in persons of unknown ages.

Cases also occurred in Portugal in 1943 and 1944 in two districts, one coastal and one inland, which were formerly the seats of epidemics. Two small epidemic centres appeared in the northern areas in 1943 and in 1944 epidemics occurred in two other northern and one south coastal area. The last comprised 19 cases only and it would have been the most serious but for prompt measures taken, since the commune concerned (Otha6) is a populous fishing and fish-canning centre.

The incidence and mortality of typhus in Portugal during the war years is shown in the following table —

Year	Cases	Deaths
1939	33	10
1940	6	6
1941	50	8
1942	18	14
1943	57	5
1944	124	21
Yearly averages 1929-1938	43.1	12.5

It is noted that unusually high death rates are recorded in 1940 and 1942, but the author attributes the low case incidence to non-notification and considers that the figures are more accurate for years when typhus occurred in epidemic form.

The yearly average for 1929-1938 was slightly exceeded in 1941 and 1943 and more than doubled in 1944. War restrictions, especially the lack of soap, are held to explain the manifestations of typhus in exposed areas.

The intensity of infection was variable. In Othað in 1944, two deaths occurred in 19 cases. Clinically, among the various degrees of intensity, it is stated that the most frequent form was "typhus *levissimus*".

The orthodox measures were taken and included isolation, delousing, organization of centres, use of 10 per cent DDT, inspection of incoming travellers and (from 1941) vaccination of sanitary staff with Cox-type vaccine imported from the United States.

H J O'D Burke-Gaffney

RAYNAL, M J H Les rats et les puces du rat dans leurs rapports avec la pathologie humaine à Chang-Hai [Rats, Fleas and Human Pathology in Shanghai] *Bull Soc Path Exot* 1947, v 40, Nos 5/6, 212-38 [39 refs]

A title such as "Rats, Fleas and Human Pathology" conjures up immediately the subjects of plague and typhus. These are undoubtedly the major concern of a health authority in conducting and continuing large-scale examination or extermination of rats. In addition to these two important infections, an opportunity was afforded of investigating other possibilities of disease transmission from rat to man. Weil's disease, sodoku, salmonellosis, rabies, and melioidosis. Actually the article returns to an old contention of the author [this *Bulletin*, 1938, v 35, 781, 1939, v 36, 464, 983 and 1940, v 37, 256, 569], with newer verification, separating both murine epizootic and sporadic endemic typhus due to murine rickettsiae which are flea-borne, from the occasional outbreaks of epidemic typhus, spreading to man from rats, but which is afterwards louse-borne. Plague as a current problem may be dismissed from consideration (though not its potential dangers in times of unusual prevalence of *Xenopsylla cheopis*), because "it seems that its local implantation is not likely to be easy" and because no case of plague has been detected in Shanghai for twenty years.

As is natural, the preliminary study relates to the rats themselves. The brains of the rats were preserved at  $-15^{\circ}\text{C}$  and, if the Weil-Felix serum test in any individual rat had given a high agglutination titre, the brain was triturated and inoculated intraperitoneally in two guinea-pigs. In some cases the material served as a test for the existence of rabies which, however, was never discovered. Other materials examined were bone marrow, urine and faeces, tested by culture for the frequency of *Proteus* and salmonellas. The rats were almost all (97 per cent) of the species *Rattus rattus* (*Epimys* black house rat) and there were almost no brown sewer rats (*R. norvegicus*). One reason for this may have been that the capture of the rats took place in a business or residential, and not in a port, area. Gravid female rats were found in greatest numbers at the end of winter and in spring. This should be the time to intensify a rat campaign. Males captured bear the proportion to females of 65.6 to 34.3. The fleas captured on rats were *Ctenopsyllus segnis*, *Xenopsylla cheopis*, *Ceratophyllus amicus* and *Ctenophthalmus felis* in the relative proportions 62.8, 26.3, 10.8, 0.1. Seasonally, *Xenopsylla cheopis* is prevalent in the warm weather of summer and autumn, and *Ceratophyllus amicus* from February to May. The former, admittedly the rat flea of plague, shows very variable prevalence, and abundance only at long intervals.

Typhus, and by this is meant classical exanthematic typhus in man, made its appearance in epidemic form in Shanghai in the years 1938, 1940 and 1942. This is a common experience in all wartime periods, and is due to crowding, misery and starvation, the disease manifested itself at an elevated endemic level.

from 1838 to 1945. A high correlation, positive or negative as the case might be with fluctuation from epidemic to endemic, was found between infected rats (diagnosed serologically) human cases of typhus and the number of rat carriers of fleas. In discussing the passage of infection from rat to man the author invokes the existence of very enzootic-epizootic murine localities and of soiled (rat-urine or rat-flea faeces) materials or virulent dust as the agents of transmission. The war conditions mentioned, when the vector becomes the louse and transmission is from man to man suffice to account for the epidemics of typhus experienced in Shanghai.

IV F Harvey

GIROUD P & JADIN J. Mise en évidence par absorption des anticorps du pouvoir antigène des tissus typhiques la éa. [Antigenic Potency of Washed Typhus-Infected Tissues shown by Agglutinin-Absorption.] C.R. Soc. Biol. 1947 June v 141 No. 11/12 579-81

By means of agglutinin-absorption reactions it was shown that crushed and washed tissues in which rickettsiae were cultivated retained a measurable quantity of antigen capable of fixing agglutinins [see this Bulletin 1945 v 42, 306]

H J O'D Burke-Gaffary

GIROUD, P & CIACCIO G. Pouvoir antigène de divers extraits de poumon de lapin infecté des rickettsies. [The Antigenic Potency of various Extracts of Rabbit Lung Infected with Rickettsiae.] C.R. Soc. Biol. 1947 June, v 141 No. 11/12 585-6.

Potent antigens were easily obtained in solution from the lungs of rabbits infected by typhus rickettsiae. Of the methods tried the most successful were making suspensions of the lungs, in 10-20 per cent. methyl or ethyl alcohol, in 50 per cent. glycerum or in 8-10 per cent. sodium chloride.

The solutions when injected subcutaneously into rabbits caused a rapid rise in the rickettsia-agglutination titre of the animals serum. The solutions, except the one made with glycerum, retained their full potency up to 70 days. After desiccation they also remained stable, with or without preliminary precipitation by ammonium sulphate.

John W D Meyer

VAN DER SCHIEER, J BOHNEIL, E. & COX, H. R. Diagnostic Antigens for Epidemic Typhus, Murine Typhus and Rocky Mountain Spotted Fever J Immunology 1947 Aug v 58 \ 4 365-75. [24 refs.]

The authors begin by giving a useful summary of the various methods of preparing antigens for the complement-fixation tests used in the differential diagnosis of epidemic typhus, murine typhus, and Rocky Mountain spotted fever.

It was found that epidemic and murine typhus vaccines prepared from infected yolk sacs by ether extraction and used as antigens gave non-specific reactions with Wassermann-positive syphilitic sera when the complement-fixation tests were carried out by the specially sensitive method of keeping the preparations at ice-box temperature for 18 hours. Little or no fixation occurred when the vaccines were purified by shaking with benzene and then concentrated by precipitation with sodium sulphate. Rocky Mountain spotted fever vaccines were treated in the same way. It then became possible to differentiate the last-named disease from epidemic and murine typhus, but in some cases epidemic typhus sera reacted nearly as strongly with murine antigen as with epidemic antigen.

In the three murine-typhus sera that were tested, the reaction against murine antigen was at a much higher titre than that against epidemic antigen.

With antigens prepared from purified and washed rickettsial suspensions by the method described by Plotz, strong cross-reactions were also observed with epidemic- and murine-typhus sera, but the titre was always higher with the homologous than with the heterologous rickettsial antigens

John W D Megaw

- i DELBOVE, P & REYNES, V Etude du comportement des virus typho-exanthématiques chez les cobayes tuberculeux [The Behaviour of Typhus Rickettsiae in Tuberculous Guinea-pigs] *CR Soc Biol* 1947, Mar, v 141, Nos 5/6, 210-11
- ii REYNES, V & DELBOVE, P Evolution de la tuberculose expérimentale chez les cobayes surinfectés par un virus typho-exanthématique [The Evolution of Tuberculosis in Guinea-pigs subsequently infected with Typhus Rickettsiae] *Ibid* 211-12
- iii DELBOVE, P & REYNES, V Etude des réactions d'immunité chez des cobayes convalescents de maladie typho-exanthématique et surinfectés avec du Bacille de Koch [Immunity Reactions in Guinea-pigs Convalescent from Typhus and subsequently infected with Tubercle Bacilli] *Ibid* 244-5
- v REYNES, V & DELBOVE, P L'allergie tuberculeuse au cours des fièvres typho-exanthématiques chez le cobaye [Tuberculous Allergy in the Course of Typhus in Guinea-pigs] *Ibid* 245-6

i The authors show that in guinea-pigs infected experimentally with human tubercle bacilli, the course of murine or exanthematic typhus, subsequently induced, differs little from the course in non-tuberculous animals, but the murine strain, which previously had failed to produce the Mooser reaction, regained its capacity to do so, as a result of passage through tuberculous animals. A tropical rickettsial strain [presumably of tsutsugamushi disease] was much less virulent to tuberculosis than to normal guinea-pigs

ii In the second paper the authors show that tuberculous guinea-pigs later infected with the three strains of typhus rickettsiae lived much longer than tuberculous controls

iii In the third paper they claim that if animals which have recovered from infection with the three strains of rickettsiae are subsequently infected with tuberculosis, there is no loss of immunity (within 3-5 months of first typhus infection) when epidemic and tropical [? tsutsugamushi] strains are considered, but that there is loss of immunity in the case of a murine strain. In each case, homologous immunity only is referred to [The numbers of guinea-pigs in each group (not more than 10) are so small that it is doubtful if the results are significant]

iv Tuberculous guinea-pigs which are infected with one of the three strains of rickettsiae after their tuberculin reactions have become positive, tend to become negative to tuberculin during the febrile period of the typhus infection, or during convalescence, but return to a positive reaction when recovery from typhus has taken place

Charles Wilcocks

DELBOVE, P & REYNES, V Recherches expérimentales sur l'évolution simultanée de l'infection tuberculeuse et des infections typhoexanthématiques chez le cobaye [Experiments on the Simultaneous Infection of Guinea-pigs with Tubercle Bacilli and Typhus Rickettsiae] *Ann Inst Pasteur* 1947, May, v 73, No 5, 439-50 [12 refs]

This is a rather fuller account of the work already reported by these authors in the four papers abstracted above. They were stimulated to conduct this study as a result of several clinical observations, but they do not state what these were

Charles Wilcocks

LEWICK, R. *Über Spätschaden nach Fleckfieber* [After Effects of Typhus Fever] *Med Klin* 1944 Aug 4 v 40 Nos. 31/32, 469-70.

Among 150 soldiers examined 4 to 12 months after attacks of typhus fever about two-thirds complained of one or more of the following symptoms — cardiac (96) irritability and restlessness (74) forgetfulness and inability to concentrate (64) headache (78) weakness (64) defects of hearing and ringing in the ears (52) and numbness of the limbs (82).

Electrocardiographic abnormalities were detected in only 14 cases, and among these there was seldom any evidence of myocardial damage. There were definite signs of damage to the nervous system in 91 cases including — exaggerated tendon reflexes (40) clonus and other spastic reflexes (34) diminished or absent abdominal reflexes (28) inequality of the pupils (45) loss of the pupal reaction to light (15) nystagmus (25) ptosis (15) facial-nerve lesions (27) hypoglossal-nerve lesions (24) Rombergism (16) diminution or loss of the knee jerk (17) tenderness on pressure over the nerves of the legs (21) sensory disturbances in the legs (18) and sensory disturbances in the arms (11).

In 32 cases, there was evidence of neuritis, mostly referred to the nerves of the legs. In 78 cases, there were indications of slight damage to the central nervous system.

In 78 cases, the cerebrospinal fluid was abnormal. In 60 of these there was an increase in the albumin and in 48 there was an increase in the cell count.

Presumably the patients had been selected for special investigation at a nerve clinic. If so the figures show only the relative frequency of the various signs and symptoms observed.

John W D Megees

WU H & WU, W P. Experimental Infection of Silkworm Pupae with Typhus Rickettsia. A Preliminary Report. *Chinese Med. J* 1947 May-June v 65 Nos. 5/6, 171-5 2 figs. & 1 chart.

Silkworm pupae were inoculated by the intracoelomic route with murine rickettsial suspensions prepared from the livers of infected mice. After the pupae had been kept at room temperature for six days, numerous rickettsiae were found in smears made from their throats. Suspensions of the intestinal and ovarian tubules of the pupae were inoculated into guinea-pigs, which developed febrile reactions similar to those caused by rickettsial inoculations.

Further study of the behaviour of rickettsiae in silkworms was impossible, because of the war situation that arose in 1944 when the experiments were in progress.

John W D Megees

WAR OFFICE. Scrub Typhus Investigations in South East Asia. A Report on Investigations by G.H.Q. [India] Field Typhus Research Team, and the Medical Research Council Field Typhus Team, based on the Scrub Typhus Research Laboratory South East Asia Command, Imphal [AUDY J R., et al.] Part I. General Account. 58 mimeographed pages of text & 11 Index pages (mimeographed) 1 map, 1 chart & 1 fig. Part II. Illustrations. Part III. Appendices (23 papers by individual workers) 1947 March. London War Office, AMD 7

This important Report deals largely though not entirely with wartime investigations carried out by a team of workers at the Scrub-Typhus Research Laboratory Imphal, near the Indo-Burma frontier.

The output of valuable work by the team was surprisingly large considering that the laboratory was fully staffed only from July to December 1945 though a few of the workers had been employed from April, 1945 and a rapidly dwindling number remained till March 1946.

Lt-Col J R Audy, R A M C, the officer in charge of the laboratory, has carried out the formidable task of editing and producing the three substantial volumes which make up the report, and readers will be surprised to find that the whole of this work was done between August 1946, and March 1947, especially as the editor himself has contributed more than half of the text and illustrations.

Lt-Col Audy craves indulgence for "many defects" in the report, but his readers will agree that these were inevitable in the circumstances and that they are trifling when weighed against the wealth of valuable material that has been made available to students of the fevers of the typhus group. Considered as a set of collected papers, the only drawbacks to the report are the relegation of the illustrations to a separate volume and the long list of corrigenda and addenda. But the report is much more than a collection of articles, as will be gathered from the following review of its contents.

#### Part I: General Report Account

The opening paper, of 19 pages, is on "The Occurrence and Identification of the Typhus Group of Fevers in the South East Asia Command". The authors are Col M H P SAYERS, R A M C, Deputy Director of Pathology, S E A C, and Brigadier I G W HILL, R A M C Consulting Physician, S E A C. The paper, written in 1945, deals chiefly with the incidence, geographical distribution, epidemiological features, and laboratory studies of scrub typhus in the Eastern Theatre during the years 1941-44. An apology is made for the use of the name scrub typhus whose only justification is its almost universal adoption, the classical name is tsutsugamushi fever.

The first outbreak recorded during the war was one of 107 cases seen in 1941 by G SINGH in a rural area of Central Burma [see this *Bulletin*, 1945, v 42, 883]. This outbreak, though definitely of the "OXK type", was suspected by Singh to be louse-borne, presumably because mite-borne typhus was not expected to occur as an epidemic.

Little is known of the occurrence of the disease in the area during 1942. Most of the outbreaks referred to by the authors as occurring in 1943 have afterwards been described in papers by their observers. They include (1) 121 cases in a battalion of a British regiment not far from Imphal, reported by TATTERSALL and PARRY [this *Bulletin*, 1946, v 43, 430] (2) 500 cases on the India-Burma border in 1943 and early 1944 reported by TATTERSALL [*ibid*, 28] and (3) 114 cases of typhus fever of which 96 were of the OXK type in an Indian Military Hospital in Calcutta, reported by Lusk [*ibid*, 246].

The only outbreak of a typhus fever other than scrub typhus mentioned by the authors is one that occurred at Ranchi in Bihar, India, early in 1943. In this, 33 persons became infected in waste-land in January 1943. Nearly all the patients gave a Weil-Felix response of the "indeterminate type", none gave an OXK reaction, and from the bibliography appended to the paper it appears that B T BOWES described the outbreak as one of "Tick-Borne Typhus".

During 1944 about 5,000 cases with 350 deaths are said to have occurred in Burma and Eastern India.

(2) In a brief paper of seven pages, entitled "The Medical Research Council Scrub-Typhus Commission", Dr R LEWTHWAITE, Director of the Institute for Medical Research, Kuala Lumpur, describes the origin and work of the Scrub Typhus Commission established by the Medical Research Council in 1944, the original members were, himself as Field Director, with Dr Kenneth MELLANBY and Charles D RADFORD as Entomologists. Dr H C BROWNING was appointed in 1945 as Experimental Biologist, but his work was interrupted by an attack of malaria followed by one of scrub typhus contracted in a

hyperendemic area in Burma. Mr H T M GORDON was appointed as associate to Dr Browning.

(3) Andy in an article of 26 pages contributes "A Review of Investigations on the Epidemiology of Scrub Typhus in South-East Asia 1945-1946." This paper which summarizes the work done by members of the staff of the Imphal Laboratory and other workers, will be found very useful by students of the typhus fevers who have not time to read the whole report. A bibliography of recent contributions on the subject of scrub typhus is appended.

(4) Andy in an article of four pages also describes "The Establishment of the Research Laboratory at Imphal (Manipur)."

(5) A Subject Index (11 pages) to the three volumes of this Report completes Part I.

#### Part II

This consists of 135 illustrations reproduced on 60 sheets of foolscap-size art paper.

#### Part III Appendices

This consists of 22 papers, of which 20 are by Lt.-Col. Andy and other members of the Imphal research team, and two are by Dr M. T. PARKER, late Major R.A.M.C. from the District Laboratory Calcutta.

Most of the papers deal with investigations carried out during the short period of existence of the Imphal Laboratory. The papers can be very roughly classified according to the chief subject matter as Epidemiological, Entomological, Bacteriological, and Survey but most of them deal with more than one aspect of the disease.

The volume contains more than 200 foolscap-sized pages in small (petit roman) type, and much of the subject matter is of a technical nature so that it is obviously impossible to do justice to each paper. Some of the articles though published with the consent of the authors, have been collated by the editor from reports and have not been revised by the workers concerned. Several of the papers are expected to be published in complete form at a later date.

#### Papers dealing chiefly with Epidemiology

In Appendix I (14 pages and 7 illustrations) Andy contributes "A Survey of Scrub Typhus in Burma, 1945." He shows that though previous records of the occurrences of the disease in Burma were scanty infection was found to be widespread throughout the country and to include such unexpected localities as waste land in urban areas like those of Rangoon and Mandalay.

In the 12th Army 598 cases occurred between March and December 1945. The proved vector was *Trombicula deliensis* and the chief animal reservoirs were *Bandicota bengalensis* and *Rattus rattus* though tree shrews and squirrels were of local importance.

Strains of *Rickettsia tsumuganensis* (now more commonly known as *R. orientalis* see this Bulletin 1943 v 40, 829) were recovered from one bandicoot and one rat, in addition to the strains isolated by Kalra from various sources including patients, and a strain earlier recovered from *T. deliensis* larvae on the Indo-Burma border.

Methods of preventing the disease in peace-time are discussed. Thorough ground clearing followed by cultivation of grazing, and rat control, are likely to be effective, but rat control must be carried out a month or two after the onset of the rains. Earlier operations may increase the risk of transmission by mites and later measures will not reduce the second generation of larvae. Personal protection by dimethyl and dibutyl phthalate and by benzyl benzoate is discussed in general terms.



In Appendix 2 (46 pages and 68 illustrations) Audy presents "An Ecological Study of Scrub Typhus". The ecological features of the disease in areas in Assam, Manipur State, Burma, Ceylon, The Maldives Islands, and India, are described in detail. Statistics of the case-incidence and descriptions of the terrain are supplied for each of a large number of infected localities in which surveys were made.

A section of the paper contains a summary of the factors concerned in the distribution of mites in relation to the ecology of the disease, and another deals with the ecology of the disease in relation to the ecology of the mites and mammals concerned in transmission. In the latter section the reader is confronted with a number of technical terms which the author mercifully defines, otherwise the uninitiated would be puzzled by such names as climatic climax, seral community, subclimax, and scrub constellation.

In Appendix 9 (5 pages) M T PARKER writes on "Scrub Typhus among Troops in the Calcutta Area in 1942 and 1943". In 1943 there were 195 cases of typhus-group fevers classified as follows: scrub typhus, 150, "X19 typhus", 23, "indeterminate" (OX2 type) 4, and "clinical typhus", 18. Most of the cases of clinical typhus were believed to be scrub typhus with a negative Weil-Felix response, and most of the "X19" cases were thought to be murine typhus. [Some of the cases of these two types and the four cases of the OX2 type may have been tick-borne.] Lusk has already discussed the features of the 114 cases of typhus seen in the Indian Military Hospital, Calcutta in 1943 (see this *Bulletin*, 1946 v 43, 426). No eschar was seen in any of the cases.

In Appendix 13 (5 pages and 1 illustration) Major S Lal KALRA, I A M C, Bacteriologist of the General Headquarters India, Research Team, and Squadron Leader C D RADFORD R A F, describe "Scrub Typhus in Ceylon". Little was known of the existence of the disease in Ceylon till the occurrence of a dramatic outbreak in which 756 persons (713 Africans and 43 British) belonging to a body of troops engaged in manoeuvres in scrub land from 11th to 15th December, 1943 were attacked within a period of seven days from the 22nd December onwards. The mortality rate was 1.3 per cent among the Africans and nil among the British. An eschar occurred in 58 per cent of the cases.

In a short summary of a paper by Radford on "Scrub Typhus Research in Ceylon" there is a statement of the infestation of bandicoots, rats, shrews, etc., by *T. deliensis* and *Ascoschöngastia indica* Hirst, 1915.

In Appendix 14 (6 pages and 3 illustrations) Kalra deals with "Scrub Typhus Investigations on Addu Atoll, Maldives Islands", and refers to the findings of Radford who collaborated with him in the work.

The most interesting feature of the disease in the small island surveyed was that without the use of mite repellents or vaccines complete control of infection was established by clearing and keeping clear the island of all low vegetation. After the initiation of this procedure there was at first a rise in the number of cases, but this was followed by a rapid fall from 33.4 per mille in 1942 to 2.4 in 1944. During the time of the survey—November 1944 to February 1945—there were no cases, and although rats and shrews infested with *T. deliensis* were found, no rickettsiae could be isolated from the tissues of 111 rats and 32 shrews which were examined. The case-fatality rate was 2.4 per cent. in 600 cases that occurred among Indian troops on the Island.

In Appendix 15 (2 pages) Kalra deals with the 'Distribution of Typhus Fevers in India'. He has already reported his findings [see this *Bulletin*, 1947, v 44, 575] but he now rightly states that the "OX19" cases presumably include "some tick typhus" in addition to murine typhus but he still bases his classification of the cases into scrub murine, and tick typhus, on the Weil-Felix response, which admittedly cannot be relied on to differentiate murine

typhus from tick typhus. [Complement fixation tests will doubtless throw light on the distribution of the typhus fevers in India.]

In Appendix 16 (7 pages and 4 illustrations) Kalra makes a "Preliminary Report of Typhus Investigations in the Kumaon Hills, United Provinces, India" during the months August to October 1946. In the country round the three small lakes of the Bhim-Tal area, 9 strains of rickettsias were isolated from 15 rats, and 5 strains were recovered from 17 batches of mites, chiefly *T. deliensis*. Many animals, domestic and wild including rats, were infested with *Rhipicephalus sanguineus* and four other species of ticks were found.

More than 2,000 ticks were collected in the region by the flag method different batches of these were inoculated into 23 guinea-pigs, of which 9 reacted 4 doubtfully and 5 definitely including 3 in which there were redness and swelling of the scrotum.

Trombiculid mites and various ticks were found on rats in five other localities, including Almora, where an average of 8 ticks was found on all the 6 rats captured and 2 of the 3 guinea-pigs inoculated with separate batches of the ticks reacted with fever and scrotal swelling.

Altogether 20 strains of *Rickettsia tsutsugamushi*: 7 tick-strains related to *Dermacentor* spp. [*Rickettsia*] *rickettsii* and one suspected murine strain, were isolated in the area of the survey.

In a later Appendix (17 dated February 1947) Kalra gives further details of the investigation of ticks in the Kumaon Hills. Among total of 20 batches of ticks from various localities 9 from Bhim Tal, consisting of *R. sanguineus* and *Boophilus* sp., and 3 from Almora, consisting of *Ixodes ricinus* caused fever and scrotal reaction in guinea-pigs and rickettsia-like bodies were found in spleen smears. Complement-fixation tests were carried out with Rocky-Mountain-spotted fever antigen on the sera of 9 of the guinea-pigs 2 of these reacted at a titre of 1-10 both were from animals inoculated with *R. sanguineus* from Bhim Tal, the others gave negative reactions.

In this appendix Kalra also reports the isolation of a similar tick strain of rickettsia from a batch of 11 ticks (*Hem. phyllis leachi* var. *indica*) found on a rat in the Imphal area in November 1946 this rat was also infested with *T. deliensis* mites but these were not infected though the host rat was found infected with *R. tsutsugamushi*.

[These remarkable findings will doubtless stimulate renewed interest in tick typhus in India. The strains of rickettsiae isolated in the neighbourhood of Bhim Tal and Almora will probably be closely studied.]

In Appendix 23 (13 pages and 6 illustrations) H. C. Brownlee and Kalra present a Report on a Scrub Typhus Outbreak in the Mandalay Area, May to July 1945.

The number of cases in this outbreak was 103 among 54 cases tested the agglutination responses were aberrant in 6 of these 3 were of the OX19 type, 2 were OX19 combined with OXK and 1 was OX19 with OX2.

A detailed survey was made of the epidemiological conditions. Laboratory mice in cages were exposed in areas in which infection had occurred among 50 mice 3 became infected with scrub typhus.

An investigation of the fauna of the soil of several localities was carried out by methods described in the paper. Trombiculids were, surprisingly absent even from the soil of places where experimental mice had become infested or infected, so that the habitat of the nymph and adult forms of the mites remained a mystery.

#### *Papers dealing with Entomology*

In Appendix 3 (18 pages and 12 illustrations) Andy discusses "The Biology of Trombiculid Mites in Relation to Transmission of Disease."

The most important observation recorded in this paper is that *T. deliensis* remains attached to its hosts for two to four days, as is the case also with *T. akamushi* of which it may be a variant. This feeding time is shorter than that of species of *Ascoschöngastia* which remain attached for about a week, and much shorter than that of *Walchia* and *Schöngastiella* which have a feeding time of about four weeks. Taking into account the infestation rates of rats in the Imphal area, it is estimated that 3,000-4,000 larvae of *T. deliensis* feed on each rat in a year, so that this mite has a great advantage over other potential vectors which have annual "turnovers" ranging from 800 to only 50 mites.

A summary of this highly instructive paper will be found in the author's Review in Part I.

In Appendix 5 (8 pages and 2 illustrations) Audy and Major H. M. THOMAS, R. A. M. C., Experimental Biologist, contribute a useful "Note on Techniques and Field Collections."

Appendix 7 (6 pages) is by Sergeant T. J. LAWRENCE, R. A. M. C., Entomologist, who writes on "Species of Trombiculid Mites in Manipur and Burma." Many new species described by the author and Radford are included, and opinions on several of these are added by Dr. Henry S. FULLER, formerly attached to the U. S. A. Typhus Commission at Myitkyina.

In Appendix 10 (3 pages) and Appendix 11 (6 pages and 6 illustrations) THOMAS deals with "Observations on the Behaviour of *T. deliensis* in Soil", and "Observations on the Development of the Nymphophane [pupa] of *T. deliensis*."

These papers will be of special interest to professional entomologists.

In Appendix 19 (5 pages and 7 illustrations) Kalra contributes "Reports on Histological Investigations" in which he describes histological techniques suitable for the investigation of mites in a field laboratory, by making serial sections. The paper includes observations on the internal structure of *T. deliensis*, on the histopathology of the eschar, and on the lesions produced in the skin of the rat by infesting mites.

Appendix 21 is by K. COCKINGS, Entomologist, who, in a short paper of 4 pages with 2 illustrations, deals with "Breeding and Trapping of Trombiculid Mites," and gives details of the technical methods employed.

#### *Papers on Bacteriology and Serology*

Appendix 8 (2 pages) is by M. T. PARKER who describes his work on "The Transmission of the infective Agent to Experimental Animals."

In December 1943, the author, working at Calcutta, isolated *R. tsutsugamushi* by inoculating the blood of a patient into the anterior chamber of a rabbit's eye. By the same method, he isolated the organism from the peritoneal exudate of three guinea-pigs which had been inoculated at Imphal (by Lt. Col. Sayers, R. A. M. C.) with pooled blood clot from several patients. Two other strains were isolated later, one from near Imphal, the other from North Burma, both from guinea-pigs inoculated intraperitoneally with blood from patients.

Guinea-pigs inoculated in this way were found very suitable for the transport of mites to distant laboratories.

In Appendix 12 (13 pages and 13 illustrations) Kalra, assisted by Sergeant J. D. BOWER, R. A. M. C., presents a "Report on Field Investigation on Scrub Typhus in Manipur, Assam."

The recovery of 19 strains of *R. tsutsugamushi* from the following sources is described—(a) From patients, 5 strains were isolated by inoculation of blood or blood clot into guinea-pigs or white mice. The patients were infected in the Imphal or N. W. Burma areas. One of the strains was recovered from the blood of Dr. H. C. Browning on the 4th day of his illness, and a sample of his blood

taken on the 18th day was examined in the U.S.A. by "Dr Sheppard [presumably C. C. Shepard], who reported a positive reaction with the complement-fixation test at a titre of 1-32 against Gilliam (Assam) antigen and at a titre of 1-512 against Karp (New Guinea) antigen. [Striking variations in the responses of the same sera to different antigens have been reported by Buxton (see this *Bulletin* 1947 v 44 61.)]

(b) From rats (six strains) from a field-mouse and a tree-shrew (one strain each)

(c) From larval mites, six strains were isolated all the batches of mites employed were collected from rats in the area south of Imphal two of the strains were from batches of mites consisting solely of *T. deliensis* the other positive batches were of mixed species, but all contained a certain number of *T. deliensis*.

Strains were also isolated from five of the laboratory white mice that had been exposed to mite attack by being placed in cages on the ground at Mandalay Fort.

Details are given of the extensive work done on the strains nine of them were maintained for 8 to 20 passages through white mice, in which their virulence usually rose during the earlier passages. Transfers of 14 strains were made from mice to guinea-pigs, in which various reactions occurred, but only one strain, originating from a tree-shrew caused peritoneal exudate containing abundant rickettsiae.

A description is given of the varied responses to inoculation of strains into seven rhesus monkeys obtained from Calcutta and regarded as free from previous infection. Some of the monkeys showed cross-immunity when challenged by a second inoculation with a different strain, but others showed no immunity or only partial immunity.

One monkey inoculated with a mite strain developed OXK agglutinins up to a titre of 1-320 (on the 34th day) this monkey was again inoculated on the 39th day with the tree-shrew strain already mentioned the response was

rise in the OXK agglutinins, whose titre became 1-1,280 on the 60th day after remoculation, and a disappearance of the OXK agglutinins. This tree-shrew strain did not protect any of four mice from death when they were challenged later by a mite strain. (No mention is made of the possibility that the tree-shrew strain might have been of the tick borne type the author states elsewhere that it resembled *R. tsutsugamushi* in its morphology and behaviour in animals.)

Local rats, though regarded as free from the risk of previous infection, were not satisfactory as test animals.

The isolation of a strain from ticks in the area has already been mentioned.

Appendix 17 (8 pages) by Kaira contains Miscellaneous Supplementary Notes, dated January-February 1947 in which the isolation of tick strains already mentioned is described. Among other recent studies are the following:—

(1) Three rats were inoculated with strains of *R. tsutsugamushi* two from Imphal and one from North Burma six months later the rats were found free from infection and were inoculated with Rhim-Tal strains of the same organism all three became infected but further experiments are contemplated to find whether infection confers lasting immunity against homologous strains.

(2) Cross-immunity tests were carried out in which rabbits were inoculated intraocularly with strains of *R. tsutsugamushi* three of which were from the Kumaon Hills, two from Ceylon, and one each from Burma and Imphal. After recovery the inoculation was repeated with strains from Kumaon five of the rabbits were found immune, but one of the Ceylon strains and the Imphal strain had conferred no immunity. Immunological differences among various strains are therefore suggested.

(3) A list of ticks collected in Imphal and the Kumaon Hills is given, these were identified by Dr M SHARIF of the Haffkine Institute, Bombay

In Imphal the commonest species was *Haemaphysalis leachi indica*, found on rats and tree shrews, the only other tick found on rats was *R. sanguineus*. In the Kumaon hills *R. sanguineus* was the most abundant, it was found on rats, dogs, sheep, cows, and horses, the only other tick found on rats was *Ixodes ricinus*, in Almora

(4) A note by Audy is included in this Appendix, it is on "An outbreak in Central India, Apparently of Tick Typhus with Eschar". Six persons were attacked in February 1945, in Bhopal State, Central India. Five of the patients had obviously been infected on the same day in a "pin-point area", and all of them had an attack which clinically and serologically conformed to the picture of tick-borne typhus with eschar. The sixth patient was infected a short distance away, he had a similar attack, but without eschar. Audy suggests that the cases with eschar may have been of the boutonneuse-fever type. He states that so far as he knows cases of tick typhus with eschar have not been reported from India. [The reviewer, about 15 years ago, saw a typical case of tick typhus in which there was a pronounced eschar at the site from which the patient had removed a tick just before the onset of the fever, this case was not recorded, the patient was seen in a hospital at New Delhi, by the courtesy of Lt Col Aspinall I M S. The presence or absence of an eschar in tick-borne typhus may be fortuitous, just as it is in scrub typhus.]

In Appendix 18 (4 pages) Kalra discusses "The Value of Proteus Agglutinins as an Endemic Index of Scrub Typhus, and in Differentiating Sub-Groups of Tropical Typhus". Sera of many animals captured at Imphal and Addu Atoll were tested for the presence of OXK agglutinins. A considerable number reacted at titres of 1-20 to 1-80, one flying fox and two lizards reacted at 1-160. Among 30 rats examined, 4 reacted at 1-80, but 4 reacted with OX19 and 2 with OX2 at the same titre. No rise in the OXK titre occurred among rats inoculated with scrub typhus at Imphal. In a small proportion of scrub-typhus patients at Imphal, Mandalay, etc, atypical reactions occurred and were verified by repeated tests, in most of these the reaction was of the OX19 type, in a few it was of the combined OX2 and OX19 type. The author states that "the clinical disease in all these cases was identical". From these and other findings recorded in the paper, and from a study of the literature, the author concludes that though the Weil-Felix test is a useful aid to diagnosis it "cannot always be relied on to differentiate sub-groups of the disease". [Complement-fixation tests might throw light on the significance of these anomalous reactions.]

#### Papers on Survey Methods

Appendix 4 (6 pages) is a preliminary report by Audy on "Applications of Air Photography to Research and Survey".

The author claims that air photography is a very useful preliminary to a survey the object of which is to avoid endemic foci of scrub typhus, and that it is also of value in the collection of information for ecological and other investigations. The numerous photographs illustrating Appendix 2 show clearly the kind of information that can rapidly be obtained by air photography.

Appendix 6 (7 pages), also by Audy, deals with "Field Surveys and Methods of Control". Concise instructions are given with regard to the methods and equipment employed in surveying known or suspected scrub-typhus areas. There is also a useful summary of the methods of controlling the disease.

In Appendix 22 (4 pages) BROWNING and GORDON describe "Methods of Field Anaesthesia in Laboratory Mice and Wild Rats". Details are given of the duration of anaesthesia resulting from the administration of several drugs in various doses. Bromethol given intraperitoneally in doses of 0.012 cc

to rats caused anaesthesia lasting about one hour. Half this dose rendered mice unconscious for about three hours. The drug had the special advantage of quick action, so that when given to animals lightly anaesthetized by chloroform or ether consciousness was not regained during the brief period needed for the production of its effect. There was also a good margin of safety.

#### Acknowledgments

Among other acknowledgments, Lt.-Col. Audy and Dr. Lewthwaite express their gratitude for helpful and friendly co-operation by Col. T. T. MACKIE and the other 13 members of the U.S.A. Typhus Commission in North Burma whose studies of the disease from December 1944 to November 1945 have already been the subject of a preliminary report (see this *Bulletin* 1946 v 43, 917 and 1132).

Dr. Lewthwaite also refers to the important work of the Australian entomologists, McCULLOCH and WOMERSLEY (*ibid.* 1945 v 42, 28, 324 and 369). Valuable contact was made with these workers and also with members of the U.S.A. Typhus-Commission team in New Guinea (*ibid.*, 901 and 933).

John W. D. Megee

KALRA, S. L. Inclusion Bodies in *Rickettsia orientalis* Infection. *Indian Med. Gaz.* 1947 June v 82, No. 6, 328-7.

In the course of his isolation of 25 strains of *Rickettsia orientalis* from various sources in 1945 the author observed homogeneous intracellular inclusion bodies similar to those described by GIROUD and PANTHER (*this Bulletin*, 1942 v 39, 753) as being associated with classical rickettsiae during their adaptation to growth in the lungs of rabbits. The author detected the bodies in epithelial cells in Giemsa-stained smears of peritoneal exudate of mice inoculated by the intraperitoneal route. The bodies were seen in only a few of the strains investigated.

John W. D. Megee

DAVIS, G. E., AUSTRIAN, R. C. & BELL, E. J. Observations on Tsutsugamushi Disease (Scrub Typhus) in Assam and Burma. The Recovery of Strains of *Rickettsia orientalis*. *Amer. J. Hyg.* 1947 Sept., 48, No. 2, 298-86.

The recovery of 85 strains of *Rickettsia orientalis* in Assam and Burma has already been described in a preliminary report by MACKIE and other members of the China Burma-India section of the U.S.A. Typhus Commission (see this *Bulletin* 1946 v 43, 917 and 1132).

The authors now give fuller details of their special investigations, including a description of the technical methods employed.

They state that Japanese workers had previously produced evidence of the occurrence of transovarial transmission of *R. orientalis* but that their own experiments were the first to demonstrate the actual presence of rickettsiae in the tissues of a host (white rat) experimentally infested with laboratory-reared offspring of infected mites (*Trombicula deliensis*). They also claim to have been the first to recover *R. orientalis* from larval trombiculid mites collected from the Yunnan buff-breasted rat (*Rattus floricolus yunnanensis*) from the large shrew (*Suncus murinus fulvo-cinnam.*) from the Assam tree shrew (*Tupaia belangeri versicolor*) and from the tissues of the above-named rat and tree-shrew.

The gerbilles—*Gerbillus gerbillus* and *G. pyramidum*—were found superior to white mice for the microscopic demonstration of rickettsiae, especially in primary isolations of the organisms.

John W. D. Megee

REDDY, D J Scrub Typhus in North Burma *Indian Med Gaz* 1947, June, v 82, No 6, 330-33

The author has made an analysis of the chief features observed in 68 patients who formed part of "nearly 100 cases" of scrub typhus treated in an Indian General Hospital at Meiktila from May to November 1946

The nationalities of the patients were Indian 38, Burmese 19, Japanese 6, and British 5 The fatality rate was 4.5 per cent, an eschar was seen in 37 per cent, adenopathy in 80 per cent, and a rash in less than 6 per cent

Apparently the diagnosis was made only in cases in which the *Proteus* OXK titre rose to 1-320 or over at some stage, in 69 per cent of the cases this titre was reached by the end of the second week One of the patients had been inoculated against the disease, his attack was mild and his OXK titre never rose above 1-320

An unstated number of inoculated persons were tested weekly after inoculation, their OXK titres were found to have "a maximum of 1-40"

During the first week, the majority of the patients showed Widal titres of 1-160 to 1-320, but during the second and third weeks these titres declined

John W D Megaw

GREENBERG, M & PELLITTERI, O Rickettsialpox. *Bull New York Acad Med* 1947, June, v 23, No 6, 338-51, 5 figs & 2 charts

This is a clear and succinct description of rickettsialpox, the interesting rickettsial disease whose very existence was not known until the middle of 1946 [see this *Bulletin*, 1947, v 44, 411, 897]

The authors give an account of the thorough manner in which the disease was investigated within a period of a few months by a team of experts, of which they were members

The only important feature of the disease that remains unknown is its geographical distribution outside the limits of New York City

John W D Megaw

SHEPARD, C C. An Outbreak of Q Fever in a Chicago Packing House *Amer J Hyg* 1947, Sept, v 46, No 2, 185-92, 2 figs [10 refs]

By complement-fixation tests a retrospective diagnosis of Q fever was made in connexion with a sharp outbreak of 33 cases of fever among 81 men engaged in slaughtering sheep and calves in a packing house in Chicago, during August, 1946

The outbreak was similar in most respects to the one that occurred in Amalhiro, Texas, in March 1946 [see this *Bulletin*, 1946, v 43, 924] There were no deaths The original clinical diagnosis in most cases was pneumonia or influenza

The patients had been engaged in handling and cutting up freshly killed animals and the highest attack rate was among those most exposed to splashing with blood and exudate from the carcasses

Droplet infection was regarded as the most likely mode of transmission of infection There was no evidence of bites by ticks or other arthropods, and no cases occurred among workers who handled the animals before slaughter

John W D Megaw

EKLUND C M, PARKER, R R & LACKMAN, D B A Case of Q Fever probably contracted by Exposure to Ticks in Nature *Pub Health Rep Wash* 1947, Sept 26, v 62, No 39, 1413-16

At the end of March 1947, a young man found himself infested by numerous ticks (*Dermacentor andersoni*) in the Bitterroot Mountains, Montana, he

crushed a number of the ticks with his fingers. Seventeen days later he became ill and suffered from headache and malaise for about 7 days.

Complement fixation and rickettsia-agglutination tests for Q fever were negative on the 8th day but on the 24th and 36th days both tests were positive. The titres observed with the former test were 1-128 to 1-512 against four different antigens, an Australian, two Italian, and the original American strain. The titre of complete agglutination of the Australian strain of rickettsiae was 1-40.

The authors state that the question arises whether infection could have been acquired through an abrasion of the skin, or even through the unbroken skin as is the case in Rocky Mountain spotted fever.

John W D Magee

## YELLOW FEVER

HOCKING, K. S. The Use of Bamboo Pots to Estimate *Aedes* Prevalence. *Bull. Entom. Res.* 1947 Aug v 38, Pt. 2, 327-33.

Various techniques have been used in attempts to estimate mosquito populations. With *Aedes* the commonest have consisted of counts of larvae or adults in houses, but these cannot be used in rural areas, e.g. around an acrodrume with no houses. The "Bamboo pot" technique gets over this difficulty. The "pots" consist of lengths of bamboo about 3 in. in internal diameter and one foot in length, filled with water and exposed in varying numbers and different localities, for periods of five days. Up to 75 per cent. were found to contain larvae in the experiments carried out. It is shown that this method of estimating *Aedes* prevalence has fewer inaccuracies than those used previously and it is particularly sensitive and valuable in well-controlled areas with few other breeding places. It can also be used in rural areas.

Kenneth McIlanby

WADDELL, Mary B. & TAYLOR, R. N. Studies on the Cyclic Passage of Yellow Fever Virus in South American Mammals and Mosquitoes. III. Further Observations on *Haemagogus equinus* as a Vector of the Virus. *Amer. J. Trop. Med.* 1947 July v 27 No. 4 471-6.

The authors first discuss the various factors which affect the chances of mosquitoes becoming infected with the yellow fever virus and their ability to transfer the infection to a susceptible vertebrate host. These factors have all been considered and investigated recently in previous papers by the authors and others working in South America [see especially this *Bulletin* throughout 1946]. They consider it virtually impossible to duplicate the conditions in any two transmission experiments and unless the conditions are the same results may vary irrespective of the vector employed.

In order to circumvent this contingency in the experiments here reported, a vector chosen as a standard for comparison was introduced and submitted to the same conditions as the vector under study. The efficiency of the latter was then determined by comparing its transmission ratio with that of the standard vector.

First the alternate cyclic passage of yellow fever virus through *Haemagogus equinus* and *Callitrix aurita* as described in a previous paper [see this *Bulletin* 1946, v 43 33 1947 v 44 309] was repeated for seven cycles. In this experiment, six to eighteen mosquitoes were allowed to feed each time.

A second experiment was carried out in which each individual mosquito was tested for virus. Infected marmosets were exposed at the same time to



normal *H. equinus* and *Aedes aegypti*. Blood was removed from the marmosets immediately before the mosquitoes fed and was tested for virus content. The mosquitoes which imbibed blood were segregated and stored in an atmosphere having a temperature of 28-30°C and humidity of 70 to 90 per cent. On 14th, 18th and 21st days thereafter they were permitted to feed individually on baby mice 2 to 3 days old. For each surviving *H. equinus* an *Aedes aegypti* that had taken the infectious meal at the same time was tested. Though the number of mosquitoes tested was small, owing to high mortality of *H. equinus*, the ratio of transmission was higher with *Aedes aegypti* irrespective of the length of incubation of the mosquitoes.

When the titre of circulating virus in the source marmoset was low at the time of feeding, few mosquitoes transmitted the infection. By this method of comparison against *Aedes aegypti*, a ratio of transmission may be obtained which should serve for comparing one sylvan species with another.

F O MacCallum

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## DENGUE AND ALLIED FEVERS

FLEMING, R F & FRENCH, J M. Dengue in Iraq. *Trans Roy Soc Trop Med & Hyg* 1947, July, v 40, No 6, 851-60.

An account of an outbreak of febrile disease in a military hospital in Iraq in late 1944 among British, Indian and Arab troops. Of a total of over 60 cases, careful clinical and pathological investigations were carried out in 24 selected on account of lymphadenitis. The results of all pathological examinations, except for the presence of an almost constant leucopenia, were negative.

In the cases selected for special examination leucocyte counts varied from 8,200 to 4,000 per cmm, no absolute lymphocytosis suggestive of glandular fever was found, and Paul-Bunnell tests were negative. *Aedes aegypti* were present in the neighbourhood. The patients usually had a sudden onset with chilliness but no rigors, the temperature rising to 104°F, severe headache, joint pains, backache and generalized aching were experienced. Severe occipital headache with pain and rigidity at the back of the neck in some cases suggested meningitis, but this was not confirmed.

The primary rash was macular or maculo-papular, appearing from the second day onwards, sometimes being so profuse as to suggest typhus, while a secondary rash, when this was present, appeared on the last day of fever and was sometimes hard to detect. The majority showed neither primary nor secondary eruption. Bronchial symptoms with widespread rhonchi were often found, the glands most commonly enlarged were the posterior cervical and epitrochlear groups. Bradycardia was almost always present.

Typical "saddle-back" temperatures were found in only three cases. The temperatures fell to normal on the 6th or 7th day, sometimes rising again to 99°-99.6°F for a few days. Albuminuria was absent.

Laboratory examinations included numerous blood smears, total and differential leucocyte counts, blood cultures, agglutinations against the enteric and *Brucella* groups, Weil-Felix reactions, Wassermann and Kahn tests, examination for leptospirae. Diagnosis was made on the clinical course of the disease, the leucopenia, and the negative laboratory tests.

[The above, though not all typical "text-book" cases, certainly appear to have been dengue or some closely allied illness. There is a group of 6- or 7-day fevers, the manifestations of which seem to vary a good deal in different

outbreaks and localities. The reviewer while in Iraq in 1920 and 1921 saw many cases of three-day (sandfly) fever but none clinically diagnosable as dengue.]

C F Shelton

## PLAGUE

SWELLENGREBEL, N. H. Interhuman Transmission of Bubonic Plague. *Bull. Office Internat. d'Hyg. Publique*. 1946 Oct.-Nov.-Dec. v 38, Nos. 10-11-12, 788-91 [French version 784-7]

Interhuman transmission of bubonic plague reduces to a consideration of the efficiency in this respect of the human flea *Palis irritans*. That it can become infected seems unquestionable as also that it can remain infected for at least 21 days. Moreover in North Africa, where this contention that plague may be transmitted by human fleas seems infestation by these fleas is of such degree as is unknown in those parts of the world where flea transmission has been very thoroughly studied, India and Java. After consideration of all the arguments, Swellengrebel comes to the conclusion that rat fleas can be carried along in cargoes and by human beings without being accompanied by rats and that antiplague measures must include disinsectionization as well as deratization, together with control of human traffic. His final pronouncement is —

Whatever the part *P. irritans* takes in plague transmission may ultimately prove to be antiumurine measures to prevent plague are highly specialised and directed against the murine population occupying human habitations only not, necessarily against other species, of rats, however important they may be from other points of view

W F Harvey

MAW, Chemotherapy in Plague. *Bull. Office Internat. d'Hyg. Publique*. 1946 Oct.-Nov.-Dec. v 38 Nos. 10-11-12, 800-807 [French version 792-9]

Part I of this communication deals with chemotherapy and consists of abstracts of reports from 1940 onwards comparing the results obtained with sulphathiazole and sulphadiazine. The control used in comparison was iodine intravenously. Part II gives the use of a broth plague vaccine originally substituted for agar because of war difficulties. The broth vaccine, acid hydrolysate of casein of Muller and Johnson, has proved by mouse protection test to be as potent as the agar vaccine is no more toxic and has the advantage of better keeping qualities.

W F Harvey

## CHOLERA

REIMANN, H. A. Further Note on the Classification of Vibrios of the 1945 Cholera Epidemic in Chungking. *Amer. J. Trop. Med.* 1947 July v 27 No 4 503.

Vibrios from several patients in the epidemic of cholera in Chungking in 1945 were classified as being of the Ogawa type in one laboratory [this Bulletin 1947 v 44 423]. Dr BURROWS of the University of Chicago examined the strains and reported different results. He has recently proposed a new classification of the cholera vibrio on a serological basis (*ibid* 422).

It would appear that, in cholera epidemics, either single type strain or different serological types of the cholera vibrio are rampant. Questions arise

as to whether (a) epidemics begin from distribution of a single type and others appear as a result of bacterial dissociation or type transformation or if epidemics are caused by one or more stable types of vibrio, and (b) if vibrios without antigen  $\lambda$ —and presumably not cholera vibrios—may cause clinical cholera, or if they are dissociant culture phase forms of pathogenic vibrios brought about by extra corporeal growth

H J O'D Burke Gaffney

YEN, C H A Differential Medium for the Isolation of *V. cholerae* Chinese  
Med J Shanghai 1947, May-June, v 65, Nos 5, 6, 133-4

In 1933, the author described a phenolphthalein starch medium for rapid isolation of *V. cholerae* [this Bulletin 1934, v 31, 44]. As this liquid medium rarely yielded pure cultures although vibriion growth preponderated he has modified it to a plate medium as follows—

A mixture of 40 cc egg-white, 280 cc distilled water and 20 cc V NaOH is beaten thoroughly, boiled gently in a basin for 30 minutes and cooled to room temperature. There are then added 100 cc of 10 per cent aqueous solution of soluble starch previously warmed to 40 C and well-shaken for 2 minutes. The volume is then made up to 1 litre with distilled water. To this are added—

Peptone	10 gm
Meat extract	3 gm
Potassium nitrate	3 gm
Sodium chloride	3 gm
Maltose	1 gm
Magnesium chloride	1 gm
Agar agar	20 gm

The mixture is heated with frequent shaking in a waterbath for 1 hour, filtered through cotton and adjusted to pH 8.0. The filtrate is distributed in 100 cc lots in flasks and autoclaved at 15 lb pressure for 15 minutes. Just before plates are poured 1 cc of 1/10,000 malachite green in 95 per cent alcohol and 0.5 cc of 1/100 rosolic acid in 95 per cent alcohol are added to each 100 cc of medium and shaken until the indicators are evenly distributed. The medium is poured into plates to a depth of about 0.3 cm. The surface of the cooled medium should not be excessively moist.

After 18 to 24 hours at 37°C, *V. cholerae* grows as transparent colonies with a clear greenish-yellow zone surrounding each one and standing out against the red background of the medium. This zone is due to the acid produced by the organism during fermentation of the starch. Various strains of common intestinal pathogens tested gave no such zone of discoloration. Staphylococci and enterococci were inhibited by the malachite green and rosolic acid. Mould contaminants could usually be distinguished morphologically and by their late appearance.

A total of 50 strains of *V. cholerae* gave the characteristic zone of decolorization but a laboratory strain of *lnaba* gave poor growth, owing to its sensitivity to rosolic acid, nevertheless it showed the zone of decolorization. The medium has been found of great practical use for some years in isolating *V. cholerae*.

H J O'D Burke Gaffney

HUANG, K W & MAO, Y C Pa-Pin (Transient Paralysis) complicating Asiatic Cholera Amer J Med Sci 1947, Aug, v 214, No 2, 153-5 [12 refs].

Pa-pin, which has been observed by the authors in 11 cases of cholera in the Chinese province of Szechuan, resembles the rare malady known as transient familial periodic paralysis. Clinical, laboratory and experimental work has pointed to barium poisoning as the cause of the malady. A further clue to the

nature of the paralysis is given in the curative action of this flaccid paralysis by administration of potassium. Although the condition is not familial in cholera nor yet a barium poisoning, it is reasonable to suppose that the pathogenesis is the same in both cases—a disturbance of potassium metabolism due to mobilization of barium from the bone reservoir as a result of dehydration and acidosis. In cholera the paralysis is late, at the time of recovery from gastro-intestinal symptoms after several days salt free diet with no drugs except non-barium containing saline infusions.

IV F Harvey

## AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

TRANS. ROY. SOC. TROP. MED. & HYG. 1947 Sept. v. 41 No 1 55-61 135 refs.] Discussion on Amoebiasis (WENYON C. M. (President), MORGAN TROYD F., MANSION-BAHR, P., STEWART G. T., O'CONNOR, R. J., MORTON T. C., GOODWIN L. G., NAPIER, L. E., HOARE C. A., ANDREW R. R., STANKUS, H. S., JONES W. R., COOKE W. E.)

Dr C. M. WENYON in his introductory remarks pointed out that interest in the subject of amoebiasis has been stimulated by great wars. This was the case during and after the 1914-1918 and also the 1939-1945 conflicts.

In the case of amoebiasis and other infections to which a large number of susceptible individuals are exposed, it is probable that the percentage of those who become infected is actually no greater than that which occurs in times of peace. The actual numbers are, however much greater in war. It is probable also that most of the cases which appear refractory to emetine or other drugs eventually recover.

There are reasons for believing that epidemics of amoebic dysentery do not occur and reference is made to the controversial instance of the Gallipoli outbreak in 1915 and the Chicago incident of 1933-1934.

It is strange that there is such little correlation between the incidence of healthy carriers and cases of amoebic dysentery. In the tropics, cases of amoebic dysentery are commoner than in colder countries and it is well understood that healthy persons, such as soldiers going overseas, amongst whom carriers occur may develop amoebic dysentery soon after arrival in the tropics, when it is safe to assume they would not have done so if they had stayed at home.

If this is due to the original strain of *E. histolytica* then it denotes that some change in the intestinal mucosa must have taken place possibly in the nature of the bacterial flora, as in the self-conducted experiments made by WESTRICH. From observations on human beings and monkeys, it is clear that the extent of invasion of the intestinal mucosa varies considerably and that sometimes, as in monkeys, when there is no visible macroscopic lesion, examination of sections microscopically will reveal that some invasion has taken place. The question whether *E. histolytica* can live in the large intestine of man without giving rise to lesions, however minimal cannot be answered. From his own experience Dr Wenyon brought forward evidence that amoebic infection can be present without giving rise to any recognizable disturbance, and can then disappear without treatment.

A point of interest is the significance of the small race of *E. histolytica*. It is generally agreed that two races do occur. The question of behaviour of this in the human intestine is difficult to decide as there do not appear to have been satisfactory records of frank amoebic dysentery in man caused by it so that we are left to surmise that the tendency to damage of the intestinal wall is less than in the large race.

As regards treatment of amoebic infections, Dr Wenyon drew attention once more to his work with O'CONNOR in Egypt during the 1914-1918 war, when the best results were obtained by giving each morning for 12 days one grain injection of emetine subcutaneously, and half a grain in capsules each evening by mouth.

Dr F MURGATROYD dealt first with diagnosis. In intestinal amoebiasis, direct microscopic examination of freshly-passed stools remains the basic diagnostic procedure. He had been unable to confirm the provocative action of emetine in diagnosis, upon which so much has recently been written, and suggested that those who had found it of value should publish the data on which their findings rest.

In his experience, the value of sigmoidoscopy or proctoscopy is slight, nor is X-ray examination of much assistance in diagnosis. The complement-fixation reaction is neither readily applicable nor reliable.

Reviewing the various forms of antiamoebic treatment, he pointed out that until recently emetine hydrochloride and emetine bismuth iodide were much less used in the U.S.A. than in Great Britain, and that in the latter country diodoquin was virtually unknown. The initial promise of combined treatment with emetine bismuth iodide and chiniofon retention enemata had not been sustained. On the question of the possible part played by concomitant bacteria in the syndrome, he finds it difficult to believe that penicillin and sulphonamide can make much difference to the total results of treating amoebiasis, since, in general, the cases refractory to treatment are not necessarily those with gross lesions. Retention enemata of emetine 1:30,000 produce results no different from those obtained with chiniofon.

It is interesting that when an emetine enema is evacuated after some hours it shows no amoebicidal activity. Of 45 patients given chiniofon enemata, 31 appeared cured, 3 relapsed and the fate of 11 is unknown. Of 53 given emetine enemata, 31 appeared cured, 5 relapsed and the results of 17 are unknown. It is suggested that the advantages gained by retention enemata in general are doubtful. To explain cases of amoebiasis refractory to treatment it is suggested that amoebae may vary in their resistance to the drugs employed, so that inadequate treatment may lead to drug resistance. Together with GOODWIN, Dr Murgatroyd has been able to bring forward evidence, by observations on infected rats, that emetine-resistance is indeed a reality. On drug metabolism we have little precise knowledge. In the case of emetine, the tests are insufficiently sensitive to follow the drug through the body. Speculations are based on therapeutic results. Thus the failure of emetine to cure amoebiasis in cats is attributed to rapid excretion in the urine. Save in a small percentage of human patients, emetine hydrochloride in doses of 1 grain daily appears either insufficient to maintain an amoebicidal medium in the tissues for a sufficient length of time to eradicate infection, or it fails to destroy the parasites in the lumen of the gut. This method, however, has been considered adequate by many in India.

The necessity of giving emetine bismuth iodide in a form in which it becomes dispersed in the gut is discussed. The addition of emetine hydrochloride parenterally in 'loading' doses at the beginning of treatment with E.B.I. may be reasonable.

It seems reasonable also to treat asymptomatic carriers of *E. histolytica* whenever possible. Dr Murgatroyd is convinced that many of the questions raised can be settled only by general agreement on the criteria for diagnosis and the necessity of further coordinated laboratory research.

Sir Philip MANSON-BAHR described the advantages of diagnosis by proctoscopy together with the variable appearances observed.

He believed that the biopsy pictures obtained from the mucous membrane are diagnostically important.

Radioecopy is of little practical value, save in amoebic typhlitis, where a peculiar filling defect of the caecum may sometimes be of decisive diagnostic value.

Dr G. T. STEWART described added bacterial infection in amoebiasis and post-dysenteric colitis. The problem of intestinal amoebiasis is twofold. Firstly there is straightforward amoebic infection and secondly the possibility of further infection by bacteria. Post-dysenteric colitis should be kept apart from the psychosomatic disorders which are grouped under "irritable colon".

The main qualitative alterations in the bacterial flora of the faeces in cases of diarrhoea due to active amoebiasis and post-dysenteric colitis are given in a table and compared with control cases. *Bact. coli* is equally prevalent in both groups, whilst paracolon bacilli and *Streptococcus faecalis* are more prevalent in the dysenteric group and statistical analysis suggests that this increased prevalence is unlikely to have arisen by chance.

*In vitro* penicillin inhibits strains of *Bact. coli*, paracolon bacilli and *S. faecalis* at concentrations ranging from 20 to 100 units per cc., but in the presence of certain sulphonamides a synergic action obtains whereby the effective bacteriostatic concentration of each drug is lowered. On this evidence, Dr Stewart has given penicillin parenterally with sulphathiazole orally to some patients and penicillin rectally to others.

Dr R. J. O'CONNOR has investigated the fate of penicillin administered rectally in treatment of amoebiasis. It was found that the first motion passed contained a large amount of penicillin at a high concentration, but subsequent motions contained little or none. The results obtained were sufficiently constant to suggest that by the rectal administration of penicillin, urinary levels of some therapeutic value might be obtained.

Air-Commodore MORROW described acute fulminating amoebic dysentery, an amoeboma simulating a neoplasm, amoebic abscess of the liver heralded by generalized urticaria, and amoebic typhlitis simulating appendicitis, with an abscess impacted in the appendix. He also outlined a course of treatment which had been found invaluable in very chronic relapsing cases. It consists of penicillin 1.5 mega units by needle + 100 gm. of sulphamockidine for the first 3 days, followed by 1 grain of emetine for 6-10 days, the latter dosage being reserved for cases in which there is leucocytosis together with the emetine, the patient received 3 tablets t.i.d. of diodoquin for 21 days. This is followed by emetine enemata (Eli Lilly & Co.) 2 tablets of  $\frac{1}{2}$  grain each t.i.d. for 10 days together with chumfon retention enema of 2½ per cent. commencing with 250 cc. and going up to 700 cc. This has proved effective in every one of his resistant war cases up to date. It has been proved conclusively by barium enema of the same consistency that with 200 cc. the splenic flexure is reached, with 500 cc. the hepatic flexure and with 700 cc. the caecum.

Mr L. G. GOODWIN showed a film recording a method of producing experimental infections with *E. histolytica* in young rats. The methods developed at the Wellcome Laboratories differ somewhat from those described by W. R. JONES [this Bulletin 1947 v. 44 313]. It has been shown that strains derived from different sources vary in their infectivity for the rat and that pathogenicity does not depend upon the number of amoebae injected, nor upon the severity of the human infections from which they were derived. It has been shown that a strain from a symptomless carrier will produce severe lesions in the rats' caecum.

Dr C. A. HOARE spoke on certain aspects of the host-parasite relationship in amoebiasis, particularly with the mode of life of *Entamoeba histolytica* in the human host. He had been able to convince himself that a certain proportion

of amoebae from cases of chronic amoebiasis have food vacuoles containing bacteria. In natural and experimental infection of macaque monkeys, *E. histolytica* behaves in most cases as a true commensal, living in the lumen of the gut and feeding on bacteria and faecal debris, and in experimentally infected rats the amoebae live as commensals, ingest bacteria, invade the intestinal wall and feed on red blood corpuscles.

The views of some authors that the amoebae living in the lumen of the gut are the only forms capable of encysting and propagating the infection need verification, whilst others have found that these forms are more resistant to the action of emetine than the tissue forms.

P Manson-Bahr

NAPIER, L E. **The Cyst-Passer** *J Trop Med & Hyg* 1947, Sept, v 50, No 9, 169-74

In an editorial article Napier discusses the significance of *Entamoeba histolytica* infections in "cyst passers". Some hold that such carriers, like diphtheria and typhoid carriers, are a menace to the community, others consider their infections invariably pathogenic, and so incompatible to perfect health in the individual, a third group regards the infection as only doubtfully pathogenic and so common that little can be done about it in practice, and a fourth believes the infection of no clinical significance if unattended by physical signs or symptoms. Stool surveys show very high rates (55.5 per cent) of infection in certain communities in the temperate and subtropical zones, and in England, some years ago, 11 per cent of a cross section of the population was found to be infected. A person may pass cysts for a year or two and then cease to do so, so the current infection-rates do not necessarily indicate the true incidence of infection in a population.

As amoebic dysentery [as opposed to amoebiasis] is essentially a tropical disease it is difficult to believe that pathological lesions are present in every case of infestation with *E. histolytica*, and the evidence in support of this contention is conflicting. *E. histolytica* can be cultured in the absence of mammalian cells, and so may live commensally in the gut of man. The theories put forward to account for its penetration into tissues include (1) variations between strains of parasites, (2) the need for a synergistic bacterial or virus infection, or (3) differences in the resistance or degree of immunity of individual hosts. Arguments for and against these are considered at some length, but none of them has been substantiated, these matters require reinvestigation.

If there is sound evidence that infection with *E. histolytica* invariably is associated with penetration of the gut tissues, routine examination of at least all sick persons in temperate climates should be done to exclude amoebiasis, and those infected should be treated. Furthermore, cyst passers in the temperate climates should be sought out and their infections eradicated in the interests of public health. The author considers it irrational to ignore the millions passing cysts in the temperate climates while treating rigorously those few symptom-free individuals in whom the infection has casually been discovered. The convalescent cyst passer in or from the tropics he holds to constitute an entirely different problem.

A R D Adams

REES, C W, REARDON, Lucy V, JONES Frances E & GRIFFIN, A M with the technical assistance of Ida L BARTGIS. **Observations on the Excystation of *Endamoeba histolytica*** *J Parasitology* 1947, Aug, v 33, No 4, 385

The senior author (*Amer J Trop Med* 1942, v 22 487) reported a micro-isolation technique for obtaining bacteria-free cysts of *Entamoeba histolytica*.

Dealing with complications the author states that the clinical course of liver abscess was typical amoebic hepatitis was often atypical, with low-grade pyrexia and often normal or slightly raised leucocyte counts, while many cases diagnosed as right pleural effusion turned out to be hepatitis and responding to emetine. Two cases of perianal cutaneous amoebiasis (this must be a rare condition) confirmed microscopically responded well to the usual anti-amoebic treatment. An interesting sequel of chronic caecal amoebiasis was found to be intestinal mal-absorption with steatorrhoea.

**Treatment**—Emetine has an immediate effect in most acute infections but when given alone it will not bring about a cure in most cases. It has no effect on cysts, but appears to be a specific in hepatitis. Emetine-resistant strains are possibly produced by indiscriminate use of this drug and its administration in insufficient doses.

**Failure of Treatment**—This may be due to —

1. Insufficient treatment. Emetine requires to be supplemented by some other drug e.g. carbamone.

2. Faulty technique. E.B.I. may be passed unabsorbed, owing to an insoluble coating in certain preparations. The stools should become a blackish colour during treatment with this drug.

3. Retention enemas (quinoxyl, yatrien etc.) containing about 2½ to 4 per cent. of the preparation, should be preceded by a wash out of about half a pint of two per cent. sodium bicarbonate solution and should consist of not more than 300 ml., given preferably by the drip method. The patient lies on his back for half an hour then on the left side for half an hour again on the back for the same period, and then on the right side for half an hour. For the remainder of the treatment (5 to 7 hours) he lies on his back.

4. Diet. A well-balanced diet, with a minimum of roughage, and no alcohol should be given. In the past patients have sometimes been underfed.

5. Undiagnosed co-existing conditions, e.g. bacillary dysentery *Giardia* and *Trichomonas* infections, malaria, kala azar.

However after elimination of all possible fallacies, a proportion of patients relapse despite all treatment.

Indiscriminate repetition of periodic courses of emetine is to be deprecated and may be dangerous. It may also possibly produce emetine-fast strains of *E. histolytica*.

Apacol, the Chinese Y a Tan Tsu, diodoquin (containing 60 per cent. iodine) have all been claimed to have had successes.

**Follow-up Procedures** —

1. Examination of at least 6 stools, three after administration of magnesium sulphate. Sigmoidoscopy and microscopic examination of specimens taken directly from suspicious areas.

2. Stool examinations as (1) after one month. Sigmoidoscopy if indicated.

3. Stool and general examination three months after stoppage of treatment.

[On page 180 the statement is made that emetine is made ineffective by heat sterilization. Many authorities will not agree with this observation.]

C. F. Shelton

PARKINSON T. Amoebiasis in Ceylon. *Lancet*. 1947 Oct. 23 612-15.

The object of this paper is to show how high is the incidence of amoebiasis in Ceylon.

The total admissions to the medical wards of an R.A.F. mobile field hospital between October 1944 and September 1945 were 635 of these 191 were for dysenteric disorders, as shown —



<i>Amoebic group</i>	97	(50.8 per cent)
Primary acute amoebic dysentery	62	
Acute relapse of amoebic dysentery	9	
Chronic intestinal amoebiasis	15	
Amoebic hepatitis	9	
Liver abscess	2	
<i>Bacillary Dysentery</i>	15	(7.9 per cent)
Cholical dysentery	14	(7.3 per cent)
Non specific diarrhoea	63	(32.9 per cent.)
Lambliasis	2	(1.1 per cent)

The reason for the relatively low incidence of bacillary dysentery is attributed to the fact that there was no epidemic, probably because the fly menace was avoided by DDT and the high standard of hygiene.

It is estimated that half the patients admitted to hospital with diarrhoea had amoebic dysentery.

The efficacy of sulphonamides in the treatment of bacillary dysentery is such that it became customary to use these drugs as a therapeutic diagnostic test, but this approach is fallacious, as the author's observations on selected cases show that sulphonamides at least mask the symptoms of acute amoebiasis and may have some amoebicidal action. It is suggested that secondary bacterial infection of the bowel may precipitate an acute attack of amoebic dysentery and be responsible for chronicity of other cases, but the rapid disappearance of *E. histolytica* from the stools in 5 cases suggests that these drugs are lethal to the amoebae. Thereafter it was customary to use a short course of chemotherapy together with emetine as initial treatment in acute amoebiasis. The following course was adopted —

Days 1-10	Emetine 1 grain
Days 1-3	Sulphapyridine (or sulphathiazole) total 14-20 gm
Days 4-13	Carbarsone 4 grains b.d.
Days 14-20	Rest
Days 21-30	E.B.I. 1-3 grains nightly (according to tolerance)

Forty-two patients with acute amoebiasis were treated on these lines. Of these it was possible to follow up 15 at an interval of 2 to 4 months after discharge from hospital. The results, both immediate and remote, have been impressive.

It is generally accepted that a leucocytosis is a distinctive feature of amoebic hepatitis, but only 5 out of 10 patients with this condition had a count of over 10,000 and others showed a moderate leucopenia. Only 6 gave a previous history of diarrhoea and in 5 of the 10 no *E. histolytica* or cysts were found in the stools.

P. Manson-Bahr

LEBON, J. MAIRE, R., DUBOUCHER, G. & CLAUDE R. Amibiase intestinale récidivante traitée par l'association pénicilline, sulfaguanidine et émétine [Relapsing Amoebic Dysentery treated with a Combination of Penicillin, Sulphaguanidine and Emetine] *Algérie Méd.* 1947 Aug-Sept, No 7, 562-4.

Account of a case

MANSON-BAHR, P. Amoebic Abscess of the Spleen *J. Trop. Med. & Hyg.* 1947, Sept, v 50, No 9, 174-5.

Generally speaking, abscesses of the spleen are extremely rare, and when they occur they are usually associated with bacterial infections.

Amoebic abscess of the spleen is of extreme rarity, and the author has been able to find but a few references to it in the literature, although most text books

refer to it. Among others, MAXWELL (*The Diseases of China* 1929 Shanghai) describes six cases in Formosa, and FRANK [this *Bulletin* 1944 v 41 572] describes one in an Indian girl.

In December 1948 the present author saw an officer from Burma, who had been invalided a year previously after 20 years service during the last 11 of which he had suffered from a marked splenomegaly believed to be malarial in origin. In 1942, in Burma, he began to suffer from increasing splenic pain. On his return to England, an abscess commenced to point in the abdominal wall in the left hypochondrium this was opened and the sinus healed spontaneously. In November 1948 the sinus reopened and discharged "anchovy-sauce" material. The spleen edge was hard and extended 4 inches below the costal margin the sinus was found to extend  $2\frac{1}{2}$  inches towards the centre of the spleen. The patient was generally in good condition without fever.

Microscopically the discharge closely resembled liver pus but no *E. histolytica* were found in it, nor were cysts demonstrated in the stools there was a leucocytosis of 10,800 per cmm. X-ray examination showed slight enlargement of the liver shadow and some elevation of the diaphragmatic dome. The left lobe of the liver was not obviously altered. No connexion with the spleen was demonstrated by lipodol injection of the sinus, a few streptococci were found in the pus from the sinus, but penicillin injections were without effect.

Emetina injections were given and the sinus began to diminish sinusul tanously the bulk of the spleen became progressively smaller on emetina bismuth iodide within a month the spleen was no longer palpable. The patient remains in excellent health.

While the aetiological agent was not demonstrated, the history and the rapid response of the abscess to anti-amoebic therapy seem to provide conclusive evidence that this was a genuine example of an amoebic abscess of the spleen.

H J O'D Burke-Gaffney

**SHERK SHIM M. Balantidial Dysentery in Rodrigues and its Treatment with Mercury Bismuth. *Brit Med. J.* 1947 Sept. 13 417-18.**

The paper describes ten cases of balantidial dysentery in Rodrigues an island 350 miles from Mauritius. Seven of the cases were in children from 3 to 13 years of age and three were in adults 30 40 and 63 years of age. One patient a man aged 30 was treated with mepacrine and a mixture of bismuth and opium. His condition did not improve and he died five days later. All the other patients were treated with bismuth of mercury (1/24 to  $\frac{1}{2}$  grain) administered intramuscularly. Two or more injections were given and in all cases a cure was obtained. The island is 40 square miles and has a population of 12,000 every household breeds at least one pig and as the hygienic conditions are unsatisfactory balantidial dysentery is to be expected. C M Wrayson

**CAMPBELL, V N & MILLER, J K. Staining Intestinal Protozoa with Iron-Haematoxylin-Phosphotungstic Acid. *Amer J Clin. Path.* 1947 v 17 733-8. [Abstract by the authors]**

A modification of Hendenhain's iron-haematoxylin method of staining intestinal protozoa is presented. The basic change is the application of 2 per cent. phosphotungstic acid for differentiation. This differentiator is automatic and

self-limiting requiring no microscopic control Uniform permanent film preparations of fecal specimens may be obtained rapidly by the modified procedure even by persons of limited experience "

## RELAPSING FEVER AND OTHER SPIROCHAETOSSES

KAMAL, A M, ANWAR, M, ABDEL MESSIH, G & KOLTA, Z *Louse-borne Relapsing Fever in Egypt A Review of 9,977 Cases* *J Egyptian Pub Health Ass* 1947, Jan, v 22, No 1, 1-22, 1 chart

The authors attempt to summarize the history of louse-borne relapsing fever in Egypt, which was first definitely recorded in the country by Sandwith and Engel in 1884, although it was probably seen by the doctors accompanying Napoleon when he invaded Egypt

The yearly incidence of the disease from 1906 to 1946 is given in tabular form For the first ten years, a few hundred cases occurred in most years and then from 1916 to 1920 there was an epidemic involving nearly 40,000 cases, after which the incidence rapidly declined and only 8 cases were recorded between 1926 and October 1944 At the end of 1944, there were 10 cases, in 1945, 18,277, and in 1946 up to September, 108,882 cases, with 2,367 deaths This great epidemic started in the Beni-Suef Province, and during 1945 spread to every part of the country except Aswan and Damietta In April 1946, the number of cases reached its peak, after which it declined and during the week ending September 30th only 25 cases were recorded

The authors compare the incidence of relapsing fever with that of the other prevalent louse-borne disease—typhus—and remark that this infection spreads more readily than relapsing fever among the inhabitants of the Delta Moreover, typhus remains endemic in the country, whilst relapsing fever disappears after each epidemic Of 9,977 cases, 6,596 were males and 3,381 females

A total of 3,011 cases were treated with one injection of arsphenamine The dose for adults was 0.60 gm given intravenously, and for children the dose was reduced according to age Of these 3,011 treated cases, 623 relapsed, whilst of 1,623 untreated cases, 1,182 relapsed Most of the relapses occurred before the 11th day of convalescence and the authors consider that patients should not be discharged until after 14 days' apyrexia from the first attack

A group of 365 cases was treated with two doses of arsphenamine on two consecutive days, and 39 relapsed Mapharside, injected for three consecutive days, was used for 371 cases and gave 27 relapses, but apart from the disadvantage of delaying the appearance of these relapses, there were other objections to its use, as it was very painful on injection, and induced rigors and vomiting

The effect of treatment on the case fatality rate is indicated in the following table —

	No. of cases	Fatality rate per cent
Untreated	245	4.5
Treated—Arsphenamine (1 inj.)	180	3.3
(2 inj.)	107	1.9
Mapharside	124	0.9

GARDHAM P. C. C., DAVIES, C. W., HEITCH R. B. & THOMAS G. L. An Epidemic of Louse-borne Relapsing Fever in Kenya. *Trans. Roy. Soc. Trop. Med. & Hyg.* 1947 Sept., v 41 No. 1 141-70 9 figs. (2 on 1 pl.) (37 refs.)

An interesting account of the first epidemic of louse-borne relapsing fever to have been recorded in East Africa. [This disease however is well known in Abyssinia and the Sudan.]

The epidemic was introduced into Kenya from South Arabia in February 1945 when a number of Arab dhows arrived at Mombasa with cases on board. It gradually spread and by October had reached epidemic proportions. In all there were about 2,000 cases in a population of 110,000 and the mortality in untreated cases was 40 per cent.

Various control measures, including the disinfection of about 100,000 people by dusting with 5 per cent. DDT powder rapidly terminated the epidemic.

The clinical features were fairly typical, but the cases were characterized by the prominence of neurological symptoms, cardiac involvement positive Weil-Felix and negative Kahn reactions. Blood examined during the initial attack nearly always showed spirochaetes, but during relapses they were often absent or very scanty.

Lice collected from patients with spirochaetes in their blood were examined both macroscopically and by inoculation into animals, but gave uniformly negative results. Subsequently lice were kept alive for 13 days after being collected. In these spirochaetes were found in large numbers and infection was produced by inoculation into monkeys. No *Ornithodoros* was ever found, and bugs collected from infected huts were negative. Attempts were made without success to transmit the infection by *Ornithodoros mombasa* and *O. sergenti*.

Rabbits, guinea-pigs, bush-babers (*Galago crassicaudatus*), white rats, white mice, gerbils and 5 species of African monkeys, were infected experimentally and showed this order of susceptibility: rabbits being the least and monkeys the most susceptible. Repeated passage in mice was easily maintained. Neurotropism hardly ever occurred.

The infections in lice showed a well-marked negative phase lasting till the 16th day and lice collected from patients and examined within 24 hours never showed spirochaetes. In view of the different results recorded in Abyssinia and China it is suggested that louse-borne spirochaetes may be divided into two groups: the first with a long negative phase in the louse including the European, North African and Abyssinian strains, and the second without this phase, spirochaetes being continually present throughout the louse cycle as in the Abyssinian and Chinese strains.

No cross immunity could be detected between *S. recurrentis* and *S. duttoni* in mice and rats but a relatively refractory bush-baby was immune to *S. duttoni* after recovery from *S. recurrentis*.

Auto-agglutination of spirochaetes in old infections occurred in monkeys but not in rats. The pathogenicity of the Kenya strain in man and animals was found to resemble most closely that of *S. carteri* and differed markedly from the Chinese and Abyssinian strains. The pathological changes resembled those previously described except that in three cases degeneration of ganglion cells was found in the cerebellum without meningo-vascular inflammation.

E. H. Mills

SHOEN, J. Considerations hematologiques en diagnostique de la fièvre récurrente. [Haematological Factors in the Diagnosis of Relapsing Fever.] *Rev. Stomatol. Méd.* Bucharest. 1947 Jan.-Apr. 36, No. 1/4 86-108, 6 figs. on 2 pls. French summary.

TOPCIU V Frecvența complicațiilor pleuro pulmonare în cursul febrei recurente  
[The Frequency of Pleuro-Pneumonic Complications in Relapsing Fever]  
*Rev Stiintelor Med* Bucharest, 1947, Jan-Apr, v 36, Nos 1/4, 129-31

The complication was found in 18 per cent of 150 patients

## YAWS

LOPES, C F Contribuição ao estudo da lesão primária da boubá. Nota  
previa [A Preliminary Note on the Primary Lesion of Yaws.] *Hospital*  
Rio de Janeiro 1945, Dec v 28, No 6 987-97, 9 figs English summary

The author believes that the primary lesion of yaws may be distinguished readily from the secondary. It is usually larger flatter, situated below the knees and causes a definite lymph gland reaction. The affected gland is slightly painful, may enlarge to the size of a pigeon's egg, but does not suppurate.

The author considers one feature to be characteristic of the primary lesion: this is a whitish areola around the lesion, in which the skin is dry rough, keratotic and furfuraceous. This areola is of variable size, may be circinate, and is seen on only one side of the lesion, "like a diadem".

He has seen this areola in about one-third of his patients with the primary lesion, but never in the secondary. The histopathological study of this feature will be the subject of another publication.

The paper is illustrated with nine photographs of lesions.

H J O'D Burke Gaffney

DWINELLE, J H, SHELDON, A J, REIN, C R & STERNBERG, T H Evaluation  
of Penicillin in the Treatment of Yaws. Final Report. *Amer J Trop*  
*Med* 1947, Sept, v 27, No 5 633-41

The authors report observations made up to 12 months after treatment with penicillin of 500 cases of primary and secondary yaws in Haiti. The schedules were: 1,200,000 units of penicillin sodium in water intramuscularly in 4 days (Series A); the same total dosage of penicillin in arachis oil and 18 per cent beeswax (300,000 units of penicillin calcium per cc) in two injections, 24 hours apart (Series B); and the same schedule as B, but 10-12 hours apart (Series C). In series B and C, dosages for children were graded down. The preliminary report has been reviewed in this *Bulletin*, 1946, v 43, 1043, where the composition of the series treated was tabulated. No severe reactions were observed, but about half of the patients in Series A had pyrexia up to 100-104°F (37.5-40°C), coming on 2-8 hours after treatment started, and lasting 10-12 hours.

Results were grouped under the following headings — "Apparent cure," with clinical cure and persistent negative Kahn tests; "Satisfactory progress," with clinical cure but progressive reduction of Kahn titre to a persistent low level, but never becoming negative; and "Unsatisfactory progress" which included "reinfections," "clinical relapse" and "serological relapse."

Patients in Series A were observed every month and those in Series B and C at intervals of 3 months. The results are shown in the following table, taken from the article —

*Primary and Secondary Yaws treated with 1,200,000 units Penicillin intramuscularly*

Series A 30 000 units in water 3-hourly for 4 days	Period of observation in months				Total Number of patients	Percent of total
	0-3	4-6	7-9	10-12		
Apparent cure (1)	0	0	5	47	52	28.7
Satisfactory progress (2)	5	5	7	106	123	65.5
(1)+(2)	5	5	12	153	175	90.2
Unsatisfactory progress	0	1	2	15	19	9.8
Total	5	6	15	168	194	
<hr/>						
Series B In arachis oil and beeswax in 2 doses 24 hours apart	3	6	9	12		
Apparent cure (1)	0	1	3	10	14	11.0
Satisfactory progress (2)	14	5	17	65	104	81.9
(1)+(2)	14	6	20	75	113	92.9
Unsatisfactory progress	0	1	5	3	9	7.1
Total	14	10	25	78	127	
<hr/>						
Series C In arachis oil and beeswax in 2 doses 10-12 hours apart	3	6	9	12		
Apparent cure (1)	0	0	1	7	8	6.4
Satisfactory progress (2)	13	10	23	62	108	86.1
(1)+(2)	13	10	24	69	116	92.5
Unsatisfactory progress	1	1		5	7	5.9
Total	14	11	28	74	125	

The higher percentage (28.7) of serological ('apparent cure') cases in Series A after 12 months may be due to the longer course (4 days) of treatment or to a change in the composition of penicillin which occurred in 1945 between the treatment of Series A and Series B and C. This is balanced by the higher percentage of satisfactory progress cases in Series B and C so that the percentages of Apparent cure and Satisfactory progress together in each Series is approximately the same i.e. 90-93. Since in Series A, children received the same dose as adults with no difference in serological response from them, it is suggested that the amount of penicillin beyond a certain minimum was not the essential factor in producing serological reversals. Duration of infection also apparently had no effect on the response to penicillin.

Of the Unsatisfactory progress cases (8.3 per cent.) at the end of 12 months in Series A, B and C respectively. Reinfection had occurred in 3.1, 1.8 and 2.4 per cent. Clinical relapses in 0.2, 4 and 0.6 per cent. and Serological relapses in 6.7, 3.1 and 4.0 per cent. Surprisingly few patients

were reinfected, 2 per cent of all the series combined, in about half of these, the Kahn titre had increased 1-2 months before the "Reinfection". Only 0.9 per cent of the series combined were "Clinical relapses". "Serological relapses" comprised 4.9 per cent.

The authors regard penicillin as the present-day drug of choice in the treatment of yaws, particularly the arachis oil and beeswax preparation, because of the short course needed and the great reduction in cases of reinfection. It should rapidly bring yaws under control.

[Even if half the "Reinfections" are included in the "Clinical relapses," their low incidence suggests that the low Kahn titres of the "satisfactory progress" cases might, for practical purposes, be regarded as negatives. As the authors observe, longer observation might support this.]

C J Hackett

TURNER, T. B., McLEOD, Charlotte & UPDYKE Elaine L. **Cross Immunity in Experimental Syphilis, Yaws, and Venereal Spirochaetosis of Rabbits**  
*Amer J Hyg* 1947, Sept, v 46, No 2, 287-95

Batches of 10-20 rabbits were inoculated intra-testicularly with *Treponema pallidum* (syphilis), *Trep. pertenue* (yaws) and *Trep. cuniculi* (venereal spirochaetosis of rabbits) respectively. Six months later they were inoculated intracutaneously with different strains of the same three species of treponema so that all possible cross-immunities could be observed. Results were compared with controls. Observations were made 21 and 35 days after the second inoculations. The tables show that there was considerable cross-immunity between all three species, perhaps less between syphilis or yaws and *cuniculi* infection than between yaws and syphilis. The protection of one infection against another is probably greater than the figures indicate, since the challenge doses were many thousands of times larger than those probably necessary to cause infection in unprotected rabbits.

It is pointed out that, in experimental syphilis, immunity is of three grades, permitting, (a) symptomatic reinfection, (b) asymptomatic reinfection, or (c) no reinfection. It depends in part upon the resistance which the host has already developed and also upon the size of the challenge dose. Although it would be unwise to carry the results of experimental work on animals into the epidemiology of yaws and syphilis in man "nevertheless, the experimental results are entirely consistent with the other evidence of a clinical, epidemiological and experimental nature, which indicates that a serviceable degree of reciprocal immunity exists between yaws and syphilis as they occur in nature." Although there is little information regarding the minimal infective doses of yaws and syphilitic treponemata for man, under natural conditions doses would probably be small so that a relatively low immunity might often protect.

An anti-yaws and anti-syphilis measure in man worthy of closer investigation might be the protection affected by *Trep. cuniculi* infection. In the authors' laboratories "at times both yaws and *cuniculi* spirochaetes produce lesions which exhibit in the experimental animal many of the characteristics of syphilitic lesions, but we have never been able to establish that this altered response signified a permanent change in any particular strain of yaws or *cuniculi* spirochaete." There is no evidence, within historical times, that syphilis has derived from yaws or *vice versa*. Perhaps, in fact, one or both of them originated from venereal spirochaetosis of rabbits or *vice versa*. *T. cuniculi* is believed to be non-pathogenic for man, but further study is needed.

Resistance of *Y. pseudotuberculosis* to challenge inoculation of heterologous strains of *T. pallidum*, *T. portusum* and *T. cuniculi* 6 months after original inoculation. Results 31 days after challenge inoculation

Original infection intratesticular	Rabbits in group	<i>T. cuniculi</i> strain A			<i>T. portusum</i> strain YD			<i>T. pallidum</i> , Nichols strain		
		Rabbits showing indicated size of lesions			Rabbits showing indicated size of lesions			Rabbits showing indicated size of lesions		
		N lesions	±	+	N lesions	±	+	N lesions	±	+
None controls	18	0	18	0	0	14	0	0	0	18
Cuniculi, strain B	18	18	0	0	0	0	0	18	2	0
Yers, strain YC	18	17	1	0	0	0	0	18	2	0
Syphila, strain S-6	18	18	0	0	0	0	0	18	2	0

Resistance of *Y. pseudotuberculosis* to challenge inoculation of heterologous strains of *T. pallidum*, *T. portusum* and *T. cuniculi* 6 months after original infection. Results 23 days after challenge inoculation

Original infection intratesticular	Rabbits in group	<i>T. cuniculi</i> strain A			<i>T. portusum</i> strain YD			<i>T. pallidum</i> Nichols strain		
		Rabbits showing indicated size of lesions			Rabbits showing indicated size of lesions			Rabbits showing indicated size of lesions		
		N lesions	±	+	N lesions	±	+	N lesions	±	+
None : controls	18	1	2	18	3	13	2	0	0	18
Cuniculi strain B	18	18	0	0	18	2	0	8	6	4
Yers, strain YC	17	8	11	1	18	1	0	14	3	0
Syphila, strain S-6	18	14	4	0	18	0	0	17	0	1

One animal of the original group died between the twenty-first and thirty-fifth day



## LEPROSY

MOISER, B Hansen's Disease (Leprosy) and Cockroaches *East African Med J* 1947, June, v 24, No 6, 230-36, 2 diagrams

This paper deals with zoological facts regarding cockroaches. The author admits that he had never seen these insects bite man, and failed to get them to do so in daylight, but he accepts statements of others to the effect that they bite at night. They are especially numerous in damp hot climates. In African huts, spraying with 5 per cent DDT in kerosene kills them in a dosage of a gallon per 100 sq feet, but the eggs are protected by a chitinous envelope, the cycle from the ova through four or more nymphal stages to adults occupies a year. A detailed description is given of the anatomy of cockroaches and it is stated that the wounds made by the chitinous mouth parts as a result of biting are characteristic, being circular or oval and varying from the size of a pin's head to 4 or 5 mm in diameter. A method of dissecting the insects is given and the appearances of acid-fast bacilli in their gut are described as in previous papers by the same author [this *Bulletin*, 1947, v 44, 725]. The occurrence of *Spirochaeta recurrentis* and *Rickettsia* in these insects is referred to, as well as helminths and certain pathogenic bacteria. L Rogers

ZANETTI, V Coloration en serie du bacille de Hansen et dépistage des lépreux bacillaires [Staining of Leprosy Bacilli and Diagnosis of Leprosy] *Ann Soc Belge de Méd Trop* 1947, Mar 31, v 27, No 1, 179-86

This paper deals with the following modification of the carbol-fuchsin method of staining lepra bacilli. First fix by heat and stain for 20 minutes with a cold solution consisting of 1 gm fuchsin, 10 cc 95 per cent alcohol, 5 cc crystallized phenol, made up to 100 cc with distilled water. Wash quickly and decolorize for 7 minutes in 0.5 per cent solution of sulphuric acid. Counterstain for one minute with a solution consisting of 0.15 gm toluidine blue, 10 cc 95 per cent alcohol, 3 gm crystallized phenol, made up to 100 cc with distilled water. Wash and dry. The bacilli are stained red with a background of violet. The acid-fast bacilli are estimated in fifty fields in five specimens taken respectively from the ear, the forehead, the cheek, a leprous plaque and from healthy skin.

The results of 2,620 such examinations are discussed. In 252 of these, clumps of bacilli were found in variable numbers in lepromatous cases. The negative cases were clinically of the nerve type, a few reacting cases of which were positive. Repeated examinations show that when very few bacilli are present they tend to disappear under treatment in four to six months, but in a few cases they increase in numbers with passage of the case into the lepromatous type. In the 252 positive cases showing clumps of bacilli, they were only found in the ears in 73, or 28.97 per cent, in both the ears and other parts in 134, or 53.17 per cent, and in the remaining 45, or 17.86 per cent, in other places only. The ear is the site of election for bacteriological examinations. This method gave better results than are obtained by hot solutions of carbol fuchsin and as good as those obtained by Hallberg's method [this *Bulletin*, 1947, v 44, 591]. L Rogers

SILVA, G Resultados de pruebas tuberculinicas en hijos de leprosos del preventivo "Amparo Santa Cruz" de Porto Alegre (Brasil) [Tuberculin Tests in the Children of Leprosy Patients in the Amparo Santa Cruz (Brazil)] *Hospital Rio de Janeiro* 1947, Aug, v 32, No 2, 163-4

The English summary appended to the paper is as follows —

"1 The tuberculin index of 121 children born from leper parents present values comparable to those of other human groups at the same ages (58.4 per

100 reactors in lepers sons and 52.9 per 100 reactors in children of an orphan asylum)

2. In 42 lepers sons non reactors to the tuberculin test, the Mitsuda reaction (leproskin reaction) was positive in 82.8 per 100

SCHUYMAN S. El valor del chanmoogra en el tratamiento de la lepra. I. Diferente evolución de los casos de lepra tuberculoides en los adultos tratados y no tratados con la medicación chanmoográfica. [The Value of Chanmoogra in the Treatment of Leprosy Course of Tuberculoid Leprosy in Adults.] *Prensa Méd. Argentina*. 1947 July 4 v 34 No. 27 1215-25 9 figs. [17 refs.] English summary

Some practitioners speak of chanmoogra with enthusiasm as to its success in the treatment of leprosy others equally detractingly of it. This divergence is explained says the author by their referring to different forms of the disease the former to the benign tuberculoid type the latter to the malignant lepromatous type.

The present article is concerned with the tuberculoid form. In infants so affected, but left untreated there is an early and spontaneous reaction against it and retrogression takes place. This is not so with adults. The author bases his conclusions on more than 400 cases seen during a period of 17 years. If untreated the primary lesion extends and secondary lesions appear or more rarely the condition remains stationary it does not clear up. If the primary lesion is excised, but no other treatment adopted, recurrence *in situ* follows. If chanmoogra is given in small doses i.e. inadequately gradual retrogression is observed, as one would expect similarly if treatment is abandoned when initial improvement occurs.

H. Harold Scott

## HELMINTHIASIS

HEAW O H. An Investigation on Schistosomiasis. *Chinese Med. J.* Shanghai. 1947 May-June v 65 Nos. 5/8 129-32.

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- That there were no known snail hosts of the parasites in India.
- That there was no infection of the local snails nor could they be experimentally infected under field conditions.
- That there were no cases of the disease among the indigenous population amongst whom the West Africans had lived in intimate contact, and using in common the same sources of fresh water stocked with gastropod molluscs.

[See this *Bulletin* 1947 v 44 599 but also 1945 v 42, 742.]

BOCARDI F. Studi sullo sviluppo e sulla struttura di *Schistosoma haematobium* nel mollusco ospite intermedio. [The Development and Structure of *Schistosoma haematobium* in its Molluscan Host.] *Riv. di Parasit. Rome*. 1947 June-Sept v 8, Nos. 2/3 67-83 10 figs. English summary

This article will interest helminthologists who wish for information on the life-history of *Sch. haematobium* and in the pathological changes which its presence and growth cause in *Bul.* and *Phys.*. The article is crammed with detail and to grasp these the original must be referred to but the findings may be summarized. Serial sections made soon after the miracidium enters

the mollusc show that penetration does not take place by the skin but by the mouth, the primary sporocyst develops and invasion of the tissues takes place and in the daughter-cysts the forked cercariae develop. Only one miracidium develops in a snail, some sort of immunity seems to prevent invasion by a second miracidium. Photomicrographs are clearly reproduced illustrating the development of the parasite and the tissue changes set up in the snail host.

H Harold Scott

BOIRON, H & KOERBER, R Contribution à l'étude de la bilharziose urinaire en Afrique occidentale française [Urinary Schistosomiasis in French West Africa] *Bull Soc Path Exot* 1947, v 40, Nos 3/4, 118-24 [13 refs]

The authors briefly review some of the work done since 1905 in French West Africa, on urinary schistosomiasis. After quoting a series of figures, they conclude that the most active foci of this disease are round Dakar, Kaolack and Fatick in Senegal, the forest region of French Guinea, the Saharan and Soudan regions of Niger, the coastal area of Dahomey, the Ivory Coast, and the basin of the Volta in the French Soudan. They mention particularly 5 foci, after noting that the disease is found along the chief water routes, whereas the coastal areas (except Dakar) are less affected. These foci are—(1) Along the Niger and its tributaries (Milo, Baoulé and Bagoé) from its source to Timbuktu (2) The old focus in Haute-Volta, associated with the Volta and its tributaries (3) The river Senegal and its tributaries (4) The rivers Gambia, Casamance and Saloum (5) Dakar. They also mention foci in contiguous areas of the British territories of the Gambia and the Gold Coast.

The authors themselves examined 580 schoolboys at Medina and 3,160 soldiers of the garrison of Dakar. In the former, 14.8 per cent showed haematuria, and in 6 per cent eggs of *Schistosoma haematobium* were found. Eggs were also found at a single examination in 13 per cent of the soldiers indigenous to French West Africa—lower rates were found in a few from the Cameroons and in 422 who originated from Madagascar. The authors, however, think that 15 and 20 per cent respectively would probably more correctly represent the incidence in the schoolboys and the local troops, arguing that a single examination cannot reveal all cases.

The authors discuss briefly some aspects of the pathology of schistosomiasis, concluding that in West Africa this disease cannot be regarded as a factor in the incidence of primary cancer of the liver. They have used intramuscular pentamidine in treatment of a few cases, with apparent success, but they have not been able to keep under observation for more than a short time the 15 patients so treated.

Charles Wilcocks

VOGEL, H Hermaphrodites of *Schistosoma mansoni* *Ann Trop Med & Parasit* 1947, Sept, v 41, No 2, 266-77, 6 figs

The author describes bisexual males of *S. mansoni*, recovered from infected laboratory animals. These worms, in addition to showing the ordinary characters of males, were provided with an ovary which, when well-developed, contained typical egg-cells. In some, a well-defined oviduct and a uterus were present, although a female genital pore could never be clearly seen. The author notes that these hermaphrodites tend to occur in less suitable hosts, such as guinea-pigs and rabbits, but not in the recognized "good hosts" such as man and monkey, and only rarely in mice; on the other hand, they occurred frequently in hamsters, which are regarded as suitable hosts in every respect. The scarcity of female worms in guinea-pigs containing hermaphrodites suggested that the absence of the female partner might be another factor in causing the development of female organs in the male.

100 reactors in lepers sons and 52.9 per 100 reactors in children of an orphan asylum).

2. In 42 lepers sons non reactors to the tuberculin test, the Mitsuda reaction (lepromin reaction) was positive in 82.8 per 100.

SCHUJMAN S. El valor del chaulmoogra en el tratamiento de la lepra. I. Diferente evolución de los casos de lepra tuberculoides en los adultos tratados y no tratados con la medicación chaulmoogrica. [The Value of Chaulmoogra in the Treatment of Leprosy Course of Tuberculoid Leprosy in Adults.] *Revista Méd. Argentina* 1947 July 4 v 34 No. 27 1215-25 9 figs. [17 refs.] English summary

Some practitioners speak of chaulmoogra with enthusiasm as to its success in the treatment of leprosy others equally detractingly of it. This divergence is explained, says the author by their referring to different forms of the disease the former to the benign tuberculoid type, the latter to the malignant lepromatous type.

The present article is concerned with the tuberculoid form. In infants so affected, but left untreated, there is an early and spontaneous reaction against it and retrogression takes place. This is not so with adults. The author bases his conclusions on more than 400 cases seen during a period of 17 years. If untreated, the primary lesion extends and secondary lesions appear or more rarely the condition remains stationary it does not clear up. If the primary lesion is excised, but no other treatment adopted, recurrence *in situ* follows. If chaulmoogra is given in small doses, i.e. inadequately gradual retrogression is observed as one would expect similarly if treatment is abandoned when initial improvement occurs.

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In order to test this theory a number of guinea-pigs, hamsters, and mice, were exposed to male cercariae only control animals simultaneously infected with both sexes of cercariae being kept for comparison. The results of these experiments were as follows—Two guinea-pigs infected with both sexes yielded 70 male worms, of which three (4.3 per cent.) were provided with a female germ-gland, whereas two guinea-pigs infected with male cercariae only yielded 83 males of which 36 (43.4 per cent.) contained an ovary. Hamsters infected in the same manner yielded similar results thus four hamsters exposed to cercariae of both sexes were subsequently found to harbour 51 male *S. mansoni* of which only one was an hermaphrodite while in contrast to these findings two hamsters exposed to male cercariae only were found to harbour 92 male worms, of which 37 (40.2 per cent.) possessed an ovary. Mice used as hosts gave quite different results, for out of 56 male worms recovered from bi-sexually infected mice, 1.9 per cent. showed an ovary whilst amongst 247 males from mice exposed exclusively to male cercariae, a smaller proportion, 1.2 per cent. were hermaphrodites.

Vogel, having shown that the appearance of female characters in the male worm is associated with development in an unsuitable host in the case of guinea-pigs and is stimulated by the absence of the female partner in the case of guinea-pigs and hamsters then discusses the causal explanation for the phenomenon. GIOVANKOLA [this Bulletin 1938 v 33 955] records the finding in a rabbit previously exposed to male cercariae only of three pairs of *S. mansoni* in copula each pair consisting of two males. The author of the present paper records similar findings at autopsies on animals infected by him with male cercariae and notes that in such instances the large worms, which play the part of the male partner contain only male genital organs, whereas the small embraced males are hermaphrodites. In view of these findings, he suggests the possibility that residence in the gynaeophoric canal, which is essential to sexual maturation of the female may likewise stimulate the development of rudimentary female characters in the male. R. M. Gordon

MOYKMAS L. Fistules à distance et indurations fécales. Séquelles de bilharziose intestinale. [Fistulae and Induration of the Buttocks after Intestinal Schistosomiasis.] Bull Soc Path. Exot 1947 v 40 Nos 3/4 86-8.

The author describes a patient who suffered for many years from a series of fistulae [sinuses might be a more accurate word] which developed on the buttocks and on the posterior surfaces of the thighs. The cause of these was obscure but in 1936 some years after the sinuses had first begun to appear eggs of *Schistosoma mansoni* were found in the faeces. Eggs were never found in discharges from the fistula though these were often examined. The mucous membrane of the rectum appeared to be normal on rectoscopy.

The Wassermann reaction was negative. Frei test was not possible, but the patient was seen by Favre himself and a diagnosis of lymphogranuloma inguinale was rejected. The author considers the conditions to be a sequel of schistosomiasis, although course of treatment with antihelmintics failed to influence the disease. Charles W. Crooks

HALAWANI A. Intensive Treatment of Schistosomiasis with Trivalent Antimony Compounds. J Egyptian Pub Health Ass 1946, Nov v 21 No. 9 219-28.

Halawani's paper begins with list of seven antimonials used in the treatment of schistosomiasis, but proves to be a reiteration of two previous papers dealing with the intensive use of Repodral, said to be identical with Fouadin.

These papers were noticed in this *Bulletin*, 1947, v 44, 220 and 329, and the present article does not appear to contain anything new William Alves

DA SILVA, L C T Tratamento da esquistosomíase de Manson pelo stiboplex  
[Treatment of Schistosomiasis mansoní by Stiboplex] *Rev Brasileira Med*  
Rio de Janeiro 1947, July, v 4, No 7, 513-17, 3 figs

The drug used, Stiboplex III, is a golden-yellow powder containing 81 per cent metallic antimony and 33.5 per cent iodine. It is soluble in a mixture of equal parts of [unspecified solutions of] sodium tartrate and urethane, and in 1 per cent propylene glycol at 24°C. The same strength in water at this temperature is not quite all dissolved.

The author gives details of experimental work with this compound on artificially infected guinea-pigs, and on its action on the worms *in vitro*. Three mgm of the drug in 1 per cent watery solution daily for 3 days killed the worms in the guinea-pigs, for the *in vitro* tests solutions were prepared varying between 0.7 and 0.0015 per cent of tartar emetic, Repodral and Stiboplex III. Even the highest dilution of tartar emetic immobilized the worms, this result was obtained by the 0.0054 per cent dilution of Repodral and the 0.0109 per cent of Stiboplex, but tartar emetic contains 0.35 gm metallic antimony per gramme, whereas Repodral contains 0.136 and Stiboplex III 0.081 gm per gramme.

Four human cases in which it was tried are detailed, all had undergone splenectomy. It will suffice to record more fully one of the four, for they are all very similar. A lad of 16 years had for some time been feeling weak and incapable of effort and complained of digestive disturbances, diarrhoea with liquid stools containing mucus, more recently a rise of temperature, palpitation, dyspnoea, the liver was enlarged, edge two fingers' breadth below the costal margin, and the spleen was enlarged to the level of the umbilicus, no malaria parasites were found. red corpuscles 3,375,000, leucocytes 4,000 per cmm, eosinophiles 6 per cent, in the faeces were ova of *S. mansoní*, *Ascaris lumbricoides*, *Necator americanus*, *Trichuris trichiura* and *Strongyloides stercoralis*. Splenectomy was performed without mishap, 7 weeks later, he was given an intravenous injection of 2 cc Stiboplex solution, three days later 3 cc, the next two doses of 5 cc at 3 day intervals, after 6 days, he was given 7 cc at 3-, 3 and 4 day intervals, all intravenously. He also had daily injections of 20 cc of 50 per cent glucose and vitamins C and B complex. After the second 7 cc dose, examination of the faeces revealed no ova of *Sch. mansoní* [nothing is said of the other infestations] and the blood showed an eosinophilia of 42 per cent [total leucocytes not stated]. In another patient, subsequent to the treatment, the eosinophiles made up 61 per cent.

The author acknowledges that four cases are too few for any generalization, but says that treatment should be "based on the principle of increasing doses at short intervals of 1 to 3 days at a rate of 10 to 12 endovenous injections, starting with 3 cc of the commercial solution to 7 to 8 cc for adults."

H Harold Scott

JANSEN, G Profilaxia experimental da esquistosomíase de Manson [Attempts at Prophylaxis of Schistosomiasis mansoní] *Mem Inst Oswaldo Cruz*  
1946, Sept, v 44 No 3 549-78, 20 figs, 1 chart & 1 map

This paper is a sequel to, or amplification of, the author's publication of 1943 [this *Bulletin*, 1945, v 42 1018]. He presents a line map of the Catende district and several photographs depicting the terrain, the construction of model baths, wash-houses and latrines. He examined, once each only, the faeces of 6,559 persons and found ova of *S. mansoní* in 3,482 (53.1 per cent). The faeces were diluted with water, passed through fine gauze, centrifuged and

the deposit examined microscopically. The results are given in age-groups. Of 651 up to 40 years of age 6.6 per cent. were positive. Of 730 between 5 and 9 years 37.1 of 780 between 10 and 14 years 68.0 of 1 607 between 15 and 24 years 71.7 of 1 158 in the next decade 61.1 after which a steady decline was observed to 35.4 per cent. of 288 over 55 years. The vector is *Anatolobes centratrialis*.

Of the drugs used for treating human cases the most successful was tartar emetic. 1,348 were thus treated and 1 159 or 85 per cent. were cured. Macleod's method was adopted. 1 per cent. solution injected *in a reman* 0.05 gm. on the first day and, if there was no appreciable reaction 0.1 gm. the next day till 0.95 gm. has been given in 10 injections. If there are signs of intolerance such as diarrhoea, nausea, vomiting and cough the dose is reduced again to 0.05 gm. The next best drug was stibetin intravenously 97 being cured out of 160 (56.8 per cent.) the same drug intramuscularly cured only 42 out of 292 (14.3) antimonyl on the other hand proved better by the intramuscular than by the intravenous route but the number treated intramuscularly was very small only 12, of whom 5 were cured of 117 injected intravenously 39 (31.1) were cured stibin intramuscularly cured 11 out of 50 (22 per cent.)

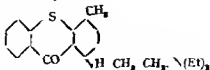
H. Harold Scott

PAX, C. Studies on Acquired Tolerance to Tartar Emetic, Antimony Sodium Thio glycolate and Neostam. *Chinese Med J Shanghai* 1946 July Aug v 64 Nos. 7/8, 181-201 4 figs. [12 refs.]

An investigation of the various factors which may produce tolerance to antimony was studied in rats and mice. tartar emetic, antimony sodium thio glycolate and neostam were used. The decrease in lethal effect of the drug following the administration of one or more initial doses in different percentages of the lethal dose and after various time intervals between the doses was used as a criterion of tolerance. In rats about 50 per cent. of the lethal dose given initially was optimal for producing tolerance and in the case of tartar emetic a single initial dose was satisfactory. In other cases, the best method of spacing the doses differed for rats and mice. If the interval between initial doses of the drug was too short a sensitivity to the substance sometimes developed. The mechanism of development of tolerance is discussed. Both tri- and pentavalent antimony compounds were found not to be cumulative in action and each type is equally effective in producing tolerance. The toxicity of tartar emetic was notably increased by starvation of the experimental animals. J. D. Fulton

LATHER, A. L. COXON R. V. & KING E. J. Measurement of the Concentration of Miracid in Biological Fluids. *Trans. Roy Soc Trop Med & Hyg* 1947 Sept. v 41 No 1 133-40 3 figs.

Miracid (1-diethylaminoethylamino-4-methyl thioxanthone)



was synthesized in Germany and gave promising results in the treatment of experimental schistosomiasis. Methods for its estimation in biological fluids are described in this paper. The fluorimetric method proved unsatisfactory. That of BRONIE & UDEKREKED (*J Biol Chem* 1945 158, 705) applied by KINCO & al [this Bulletin 1946 43 822] to the estimation of paludrine by taking with a dye was tried by the present authors but has not been fully developed.



They finally adapted a simple colorimetric method, in which the yellow colour produced by miracid extracted from 5 ml of blood and dissolved in 0.04 N HCl was read in a Spekker absorptiometer with ultra-violet light and special filter. By this means, 10 to 100  $\mu\text{g}/100\text{ ml}$  could be estimated. After the blood was haemolysed by distilled water, the mixture was made alkaline and then extracted twice with ether, which was in turn washed with alkali and water, and then extracted with HCl of definite concentration before readings were made in the absorptiometer. The amount of miracid present was determined from a calibration curve. Recoveries of miracid added to blood varied from 80 to 110 per cent. Similar results were used for estimating miracid in urine and the error was not greater than 10 per cent.

J D Fulton

PESIGAN T P TORRES, L F, Jr & RECIO P M Paragonimiasis Westermani  
an Unexpected Case with Cystic Formation in the Anterior Abdominal Wall  
*J Philippine Med Ass* 1947 July, v 23, No 7, 293-8 2 figs on 1 pl

WU, K Fasciolopsis in Guinea Pigs with a Summary of the Definitive Hosts  
*Chinese Med J Shanghai* 1946, July-Aug, v 64, Nos 7/8, 219-23,  
4 figs on 1 pl

Experimental feeding of *F. buski* cysts to 16 guineapigs gave one positive result, in which immature worms were found in a guineapig which died prematurely. From this and previous investigations it is concluded that these animals are probably not suitable for laboratory work with *F. buski*. Previous work, by the author and other authorities, on the definitive hosts of this worm is summarized in a table.

J J C Buckley

VON BONSORFF, B Does Feeding of *Diphyllbothrium latum* Influence the  
Interaction between the Intrinsic and the Extrinsic Factors of Castle?  
*Diphyllbothrium latum* and Pernicious Anemia VIII *Acta Med Scandi-*  
*navica* 1947, Oct 15, v 129, No 1, 59-76, 8 figs

"The addition of fresh or dried *Diphyllbothrium latum* has not the power to nullify the antianemic effect of mixtures of extrinsic and intrinsic factors when given to patients with cryptogenetic pernicious anemia, the administration of dried worm does not hinder the remission after worm cure in pernicious tapeworm anemia, and the admixture of dried worm to hog's stomach preparations does not diminish their therapeutic effect."

ALLEN, R W The Thermal Death Point of Cysticeri of *Taenia saginata* J  
*Parasitology* 1947, Aug, v 33, No 4, 331-8 [11 refs]

"1 A series of experiments was carried out to determine the thermal death point of cysticeri of *Taenia saginata*. After the cysticeri were exposed to various temperatures, attained gradually, they were tested for viability by the use of one or all of the following criteria: (1) ability to evaginate in warm sodium taurocholate solution, (2) activity of flame cells, and (3) the ability to pass through the digestive tract of man without being digested.

"2 Decapsulated cysticeri heated to temperatures as high as 54°C evaginated partially in sodium taurocholate solution and showed active flame cells in some cases. A small percentage of those heated to 55°C evaginated partially in taurocholate solution but none showed active flame cells. Those heated to 56°C did not respond in taurocholate solution, did not show active flame cells, and were completely digested when passed through the digestive tract of a human subject.

3. Cysticerci that were heated in muscle tissue to temperatures as high as 50°C. evaginated in taurocholate solution and showed active flame cells. A small percentage of those heated to 55°C. evaginated partially but none showed active flame cells. However 3 out of 6 were not completely digested when passed through the digestive tract of a human subject. Cysticerci heated gradually in muscle tissue to temperatures of 56°C. and those that were heated to 57°C. did not respond in taurocholate solution, did not show active flame cells, and were digested when passed through the digestive tract of a human subject.

SURRACO, V. L. & GALEANO MUÑOZ, J. Primer caso documentado, en el Uruguay de parasitismo humano por *Hymenolepis diminuta*. [First Recorded Case in Uruguay of Human Infection with *Hymenolepis diminuta*.] *Arch. Uruguayos de Med. Ciruj. y Especialidades*. 1947 Apr. v. 30, No. 4 370-78, 5 figs. [10 refs.] English summary (5 lines)

A case in child aged 4.

LARSEN, J. E. Jr. The Role of Reduced Food Intake in Alcoholic Debilitation of Mice Infected with *Hymenolepis*. *J. Parasitology* 1947 Aug. v. 33 No. 4 338-44.

A suggestion that malnutrition, brought about by alcoholic debilitation, may have been an important factor in weakening the resistance of young mice to infection with *H. nana* var. *fraterna* as previously demonstrated by the author [this Bulletin, 1946 v. 43 759] led to the present studies. Having demonstrated that alcoholic mice consumed much less food per day than non-alcoholic controls, the latter were forced to fast daily during the experiment so that their food intake was about the same as that of the alcoholic mice, and after infection they showed a percentage development of cysticercoids which was about the same as that of the alcoholic mice but considerably higher than that of the non-alcoholic, non-fasting controls. Thus the effect of the alcohol in reducing resistance to *Hymenolepis* infection is indirect and operates by interfering with the normal food intake. Subsequent tests showed that this reduced resistance was mainly due to avitaminosis. J. J. C. Buckley

LARRIER, E. P. ARDAS, H. A. & CAMINELLI, J. F. Estudio del tejido de granulación de la adventicia de un antiguo quiste hídatico del hígado operado. [Structure of the Granulation Tissue in the Adventitia of an Old Operated Hydatid Cyst of the Liver.] *Arch. Uruguayos de Med., Ciruj. y Especialidades*. 1947 Apr. v. 30 No. 4, 399-414 6 figs.

YANA, CILL, R. SUAREZ, H. & CASTRO CASAL, H. Granuloma hídatico pulmonar en el adolescente. [Hydatid Granuloma of the Lung in an Adolescent.] *Arch. Uruguayos de Med., Ciruj. y Especialidades*. 1947 Apr. v. 30 No. 4 391-3, 5 figs.

VALEDES RUIZ, M. & SALAS LUNA, E. Quiste hídatico del bazo. [Hydatid Cyst of the Spleen.] *Med. Colonial*. Madrid. 1947 Oct. 1 v. 10 No. 4, 207-20 1 fig.

CELEKIER, D. & ORLANDI, M. A. R. Hidatidosis abdominopelviana. [Abdomino-Pelvic Hydatid.] *Proceso Med. Argentina*. 1947 July 11 34 No. 28, 1298-92, 2 figs. [37 refs.]

Report of a case.

BENAIM PINTO, H Aspectos cardio-vasculares de la anquilostomiasis, con especial referencia al problema de la miocarditis crónica [Cardiovascular Disturbances in Ankylostomiasis, with special reference to the Question of Chronic Myocarditis] XII Conferencia Sanitaria Panamericana Cuadernos Amarillos Publicaciones de la Comisión Organizadora No 26 Caracas 1947 452 pp, numerous illustrations [Bibliography]

This exhaustive work was presented as a thesis for the M D degree of the Central University of Venezuela. The question of chronic myocarditis is a serious one in Venezuela, its causes are several and the problem is not purely medical but also economic and social. Circulatory disturbances arise in part from dietetic causes, in part from syphilis, in part from trypanosomiasis (Chagas's disease), in part from schistosomiasis, and in part from ankylostomiasis. The last is dealt with fully in this thesis, the first also comes into play in association with hookworm disease, the other known causes receive mere casual mention.

It is estimated that there are some two million persons in Venezuela harbouring hookworms, more than half the total population, and the concomitant circulatory disturbances are of general clinical importance and of interest to many others than specialists and cardiologists. Some of the associated symptoms have been ascribed hitherto to "hookworm anaemia", but much of the cardiac distress, perhaps to a degree resulting in death, is due to myocarditis.

This volume takes up and discusses minutely various aspects of the problem, mostly with quotations or abstracts from other authors. There are more than 500 references in the bibliography. The author's observed cases numbered 28, their ages ranged between 8 and 70 years, only six were children, 17 were males, 11 females—all the men were agricultural workers, the women did domestic work, occasionally helping in the fields. The degree of anaemia was severe—red cells 960,000 to 2,960,000 per cmm, with an average of 1,759,350, haemoglobin 10–50 per cent, average 29, six were suffering from schistosomiasis and others had syphilis also, only 14 could be considered as suffering from uncomplicated hookworm myocarditis. The commonest symptoms were dyspnoea, praecordial oppression, vertigo, tinnitus and headache, oedema, pulsating jugulars, hydropericardium in one patient, hydrothorax in two [recorded as 3.5 and 7 per cent respectively], anasarca in six, gallop rhythm in eight. The chief pathological change in the heart was a fatty degeneration referable to the anaemia, with cellular infiltration, interfibrillar oedema and increase of connective tissue—all non-specific. Secondary hepatic lesions were naturally present. Each of the 28 cases has a detailed report, with, in most instances, reproductions of the electrocardiograms which are very clear, and X-ray photographs of the thorax, less clear.

H Harold Scott

LIE KIAN JOE *Trichostrongylus* Infection in Man and Domestic Animals in Java *J Parasitology* 1947 Aug, v 33 No 4 359–62

Post-mortem examinations of 119 Indonesians and 32 Chinese revealed *Trichostrongylus* infections in 49 and 6 respectively. *T. colubriformis* was present in every positive case while *T. axei* was found 11 times, in Indonesians only. The number of worms in one individual is usually very small, but in one instance over 5,000 were collected. The duodenum and upper part of the jejunum are the most common habitats.

Experimental infections of a human volunteer were carried out, with larvae of *T. colubriformis* cultured in faeces of a naturally infected goat. These were successful by the oral method, but cutaneous exposure gave negative results.

Similar experiments with *T. axei* were negative. Young goats were easily infected with *T. colubriformis* larvae from human sources both in this and in the human experimental infection 21 days elapsed between exposure and first appearance of eggs in the stools.

No symptoms of sickness accompanied the human infections, but there was a transient eosinophilia to 10 per cent.

J. J. C. Buckley

FAIN A. Répartition et étude anatomo-clinique des filarioses humaines dans le territoire de Banningville (Congo Belge). (*Wuchereria bancrofti*—Cobbold, *Filaria loa*—Guyot, *Dipetalonema perstans*—Manson, *Dipetalonema streptocerca*—Macfie et Carson *Onchocerca volvulus*—Leuckart) [Survey and Anatomical and Clinical Study of Human Filariasis in Banningville (Belgian Congo)] *Ann. Soc. Belge de Méd. Trop.* 1947 Mar 31 v 27 No 1 25-63 7 figs. [22 refs.]

The observations upon which this paper are based were made in the Banningville Territory (Belgian Congo) which is situated between 16 and 19° long. E. intersected by 4° lat. S.

The territory is watered by important rivers of which the principal are the Kwango to the east and Kasai to the west. The population is sparse grouped in villages and hamlets of 100-200 persons. Two thousand five hundred Africans were examined, and these comprised about one-tenth of the adult population. Thick blood-films stained by Giemsa were employed.

A focus of *W. bancrofti* of the periodic type producing clinical manifestations described in other endemic regions was studied for the first time in the Belgian Congo along the course of the Kwango river. The endemic area is confined to the course of the larger rivers.

Several specimens of the adult stage of this worm were obtained for the first time in the medical history of the Congo. The females were entwined in association with the males, usually enclosed in cavernous tissue; the males, on the other hand, were often found free and extended, making their way through healthy tissue; thus, several were discovered in the centre of the testis.

Adenopathies and lymphatic varices, and hydroceles were most frequently encountered, and elephantiasis affects about 4 per cent, with predilection for the lower extremities. Filarial lymphangitis was not encountered.

Several small endemic foci of *Onchocerca volvulus* were discovered in Banningville territory. The only clinical signs observed were cysts or nodules almost exclusively confined to the iliac cysts.

There appears to be no relation between the presence of subcutaneous cysts and the presence of *O. volvulus* microfilariae in the skin. About twice as many people harboured microfilariae in the skin as did those who exhibited cysts. On the other hand, cysts containing viable microfilariae may be present and at the same time the latter may be absent from the skin.

Of greater interest is the discovery of *Dipetalonema streptocerca*. This classification is adopted on the authority of PIERI and CHARDONNET [this *Bulletin* 1947 v 44, 339] who have shown that the parasite of the chimpanzee is almost identical with that of man. The distribution of this filaria is regulated by little-known factors. On the whole it predominates in the south, but it is also found along the course of the Wamba and Kwango rivers. No clinical manifestations were observed in association with this parasite. It may possibly be coincidental that it is closely associated with goitre.

*Acanthocheilichthys perstans* is uniformly distributed amongst the native population. The average percentage may be as high as 60. The riverside villages are more heavily infested than those more remote from the larger rivers.

No clinical manifestations were observed

*Loa loa* is rare in the territory, and the few cases encountered were probably imported. This is probably explained by the absence of the insect vector

P Manson-Bahr

DILLER, W F Notes on Filariasis in Liberia *J Parasitology* 1947, Aug, v 33, No 4, 363-6

Diurnal and nocturnal blood surveys for filariasis were carried out on Liberian natives. Blood smears taken by day from 2,134 persons gave 14 cases of *Wuchereria bancrofti* and 2 of *Acanthocheilonema*, while those taken at night from 955 showed 8.7 per cent positive for *W. bancrofti* and one case of *A. perstans*. Many cases of elephantiasis were observed, of which scrotal enlargement was the principal type. A blood survey of 431 American soldiers who had been stationed in Liberia for a year or more proved negative for microfilariæ.

Dissections of 649 mosquitoes, mostly *Anopheles gambiae*, gave evidence that this species is the probable vector of *W. bancrofti* in the area

J J C Buckley

CULBERTSON, J T, in collaboration with H M ROSE, HERNANDEZ-MORALES, F, OLIVER-GONZALEZ, J, FIGUEROA ORTIZ, L, RUIZ REYES, F & NETTEL, R. Experimental Chemotherapy of Filariasis. *Trans Roy Soc Trop Med & Hyg* 1947, Sept, v 41, No 1, 18-43, 1 pl & 1 chart [11 refs]. Discussion 44-54, 1 chart [WENYON, C M (President), ROGERS, L, NAPIER, L E, HAWKING, F, FAIRLEY, N H, MANSON-BAHR, P, GOODWIN, L G, JOHNSTONE, R D C, CULBERTSON, J T (in reply)]

CULBERTSON gave an account of the experimental work done by himself and his colleagues on the chemotherapy of *Litomosoides carini* infections in cotton rats (*Sigmodon hispidus*), of *Wuchereria bancrofti* infections in man, of *Loa loa* infections in man, and of *Onchocerca volvulus* infections in man.

In cotton rats, naturally infected with *Litomosoides carini*, it was observed that intensive treatment with pentavalent antimony cures the infection [see this *Bulletin*, 1944, v 41, 772 and 1947, v 44, 229]. The adult worms live in the pleural space of the rat, and microfilariæ occur in the blood. Antimony compounds, such as neostam, neostibosan, and solustibosan, kill the adult parasites in 2 weeks or less, as shown by autopsy, a single massive dose of the drugs often being effective in this, microfilariæ, however, linger in the blood, possibly after a temporary drop in number, for months, but once they vanish they do not reappear. The adult worms are evidently much more vulnerable to treatment than are the microfilariæ. On this important observation is based a re-examination of the drug treatment of the human filariases.

One hundred and twenty-nine Porto Ricans, shown to be infected with *W. bancrofti* but only 3 of whom had clinical evidence of their infections, were variously treated with 4 pentavalent antimony compounds (neostibosan, neostam, urea stibamine and stibanose), with 3 trivalent antimony compounds (fouadin, anthiomaline and tartar emetic), and with an arsenical (melarsen oxide) [see this *Bulletin*, 1946, v 43, 54, 354, and 763]. Microfilarial counts were made on each patient, at a fixed hour, in 60 cmm of nocturnal blood, when these failed to yield microfilariæ, 10 cc of blood were examined by a concentration technique. Fifteen control persons were similarly observed. These latter continued to show microfilariæ throughout the period of observation, but in those cases treated with the drugs, microfilariæ vanished in a considerable number of instances after some months. The results of treatment are summarized in the following table —

Drug	Number of patients treated	Number of patients freed of microfilariae
Neostibosan	35	23
Neostam	11	5
Urea stibamine	8	4
Stibanoes (Solustibosan)	5	1
Foundin	15	3
Anthracmaline	20	7
Tartar emetic	4	0
Melarsen oxide	18	8

The drugs were given in high dosage to produce these results and some of them especially foundin produced severe drug reactions. neostibosan was the most satisfactory and was well tolerated. The blood levels of antimony attained with the various compounds did not bear a constant relationship to the successful eradication of the infection and the destruction of the adult worms did not lead to elephantiasis or other physical signs of filariasis in the patients. The author does not consider that any of the drugs tried so far are ideal agents for therapeutic use and he recommends caution in treatment, lest this prove more hazardous to the patient than the infection.

Three patients suffering from *L. loa* infections all of whom had, or had had Calabar swellings, but only one of whom had microfilariae in the blood, were given an intensive course of neostibosan for two weeks. The two patients with recurring Calabar swellings ceased to suffer from these and the one with microfilariae, but no current swellings, 15 months later had only 8 per cent. of the number present before treatment.

Forty Mexican patients with onchocerciasis nearly all of them with severe ocular manifestations, three being blind, were divided into two equal groups. One of these groups was treated intensively with neostibosan intravenously for two weeks and the other was kept as a control. Several of these patients towards or after the end of the course of treatment became frankly ill as a result of it, and one died 3 days later with evidence of renal damage. None of the controls was ill. The estimation in these patients of the levels of their infection rested on counts of microfilariae in skin snippings taken from each cheek and each side of the neck, irrespective of the size of any nodules which might be present. As a result of the unfortunate fatality it proved difficult to follow the cases adequately however one patient was studied for 5 months, and seven others for 10 months. On comparison with the controls it is difficult to find any evidence of permanent effect of the treatment on the microfilarial levels of *Onchocerca volvulus* in the skin snippings of these patients.

[This paper should be consulted in the original by those interested. It contains detailed information that it is impossible to summarize the dosages of the drugs used, and other relevant data, are set out in numerous tables and charts.]

In the discussion which followed, Rogers recapitulated his pioneer observations on the treatment of *W. bancrofti* infections with sodium antimony tartrate [see this Bulletin 1920 v 15 234 and 1921 v 17 85] and he now thought that CULBERTSON's demonstration of the lengthy survival of microfilariae in the blood after successful treatment confirmed his original belief that he had successfully destroyed the adult worms in his cases. He then discussed the aetiology of the periodical attacks of febrile lymphangitis which are a feature of Bancroftian filariasis. After summarizing the records in the literature on the

drug treatment of this infection, he suggested that ALVES and BLAIR's intensive treatment with trivalent antimony salts [see this *Bulletin*, 1946, v 43, 344] was worthy of investigation in this connexion

NAPIER recorded some experiences in the treatment of filariasis over 25 years in Calcutta. He concluded that a number of cases of filariasis suffering from kala-azar must have been cured of their infections by the antimonials employed in the treatment of the latter disease. He thought the failure to demonstrate the curative action of these drugs in his cases of filariasis was due to the fact that examinations were not pursued for sufficiently long to recognize that cure had been achieved.

HAWKING referred to the treatment of filariasis in E. Africa with various compounds, more particularly foudadin which was pushed to the toxic limit, and considered that the failure to appreciate the effect of these compounds was attributable to ignorance as to the longevity of microfilariae, a subject on which light had now been thrown by CULBERTSON and his colleagues. He remarked on the ease with which *Litomosoides* infections can be maintained in cotton rats in Britain through the vector mite, *Liponyssus bacoti*, and referred to the infectability of ordinary laboratory rats, mice, hamsters and Orkney voles, but he considered these unsuitable for chemotherapeutic work as the infections are light, and tend to die out spontaneously. He made some observations on the activity of various compounds on experimental filarial infections, and stated he had found arsenical compounds even more active than antimonials, and that half-grown immature worms are much more resistant to drugs than fully-grown worms, which might account for some of Culbertson's failures to cure.

HAMILTON FAIRLEY, MANSON-BAHR, GOODWIN, and JOHNSTONE also contributed to the discussion. In reply, CULBERTSON dealt with some of the many points raised and concluded with extracts from Manson's diary, written in 1892-93 suggesting that Manson had demonstrated some therapeutic action of thymol in a case of filariasis carefully observed at intervals for 12 months.

A. R. D. Adams

WILARTON, D. R. A. Pathological Changes in Natural and Experimental Filariasis in the Cotton Rat. *J. Infect. Dis.* 1947, May-June v 80, No 3, 307-18, 15 figs. [18 refs.]

"Pathological changes in the cotton rat *Sigmodon hispidus*, infected with the filarial worm, *Litomosoides carinii*, are here described. The only clinical sign associated with the infection is a palpable spleen. The infection gives rise to the formation of papillary nodules that may cover the visceral and parietal pleura. The nodules arise from a proliferative edematous reaction of the pleura followed by infiltration of lymphocytes, neutrophils and eosinophiles, and, later, plasma cells and fibrocytes. Thick laminated fibrosis and enlargement of the lymphatics of the pleura occur in heavy infections.

The lung tissue shows scattered eosinophilia and hypertrophy of the lining alveolar cells. Eosinophilia is characteristic of the pulmonary blood but not of the peripheral blood. The larger bronchioles may be involved in a markedly eosinophilic edematous reaction suggestive of asthma.

Living microfilariae are numerous in the pulmonary vessels but are not centers of reaction. The size of the spleen is two and one-half times that of the normal organ. The spleen shows follicular hyperplasia. *Bartonella* has not been observed. Peritoneal and occasionally inguinal lymph nodes may be enlarged.

The differential white blood cell count appears essentially unchanged.

Adult worms may migrate through the mediastinum or be immobilized and destroyed there.

The pathological effects here recorded have been reproduced experimentally in normal cotton rats. The reaction in the host seems to be due primarily to excretions of the living adult worms and not necessarily to the disintegration of dead worms. Circulating living microfilariae appear to have little if any effect. The reaction is characterized by edema and eosinophilia and is considered to be predominantly allergic.

The significance of these findings in relation to the pathological changes in human filariasis and elephantiasis is discussed."

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## DEFICIENCY DISEASES

KODICK, E. CARPENTER, K. J. & HARRIS, L. J. "Pellagrasis" Astoria of Malawi. Further Experiments. *Lancet*. 1947 Oct. 25 616-17 [12 refs.]

In 1946 the authors reported (*this Bulletin* 1947 v 44 119) that growth-rate in rats is retarded by the addition to their diet of indole-3-acetic acid, a substance of which a precursor is present in significant amounts in maize. This effect was counteracted by the addition to the diet of either nicotinic acid or tryptophane.

In subsequent trials, these results have not been consistently reproduced. A number of control animals on the basal diet have shown depression of growth and the proportion of rats on the indole-3-acetic acid diet showing retardation is no longer significantly greater than in the control series. Other workers have experienced similarly irregular results.

Rats given a 40 per cent. maize diet do, however, show the same retardation curable by nicotinic acid or tryptophane, as was previously observed.

In the search for a possible toxic factor in maize the maize-meal was extracted by a procedure designed to remove the indole-3-acetic acid and which, at the same time removed a protein fraction. Rats fed on the extracted meal showed little or no growth retardation. Feeding experiments with the extract and with fractions derived from it have so far given inconclusive results.

It is suggested that the erratic responses observed by several workers in this field may be due to change in the bacterial flora of the intestines and consequent change in microsynthesis, possibly brought about by the prolonged use of synthetic diets.

The present findings make it seem very unlikely that indole-3-acetic acid can be responsible as such for the apparently more constant pellagrasis activity possessed by maize.

Dean A. Smith

PÉREZ, J. C. La pelagra en la República de Bolivia. [*Pellagra in Bolivia.*] *Hospital* Rio de Janeiro. 1945 Oct. v 28, No. 4 543-57 English summary

A general account of pellagra the origin of its name, the history of the disease, its causation and symptomatology followed by the narration of a case in a man of 35 years in Cochabamba, who is believed to have contracted the disease owing to the low diet resulting from the war between Bolivia and Paraguay. Cure was obtained rapidly from administration of nicotinic acid in tablets of 0.05 gm. taken twice daily before the principal meals, in combination with injections of liver extract (form and dose not stated) which the author thinks is a valuable adjuvant to the nicotinic acid. H. Harold Scott



## SPRUE

- 1 FRAZER, A C *Aetiology of Steatorrhoea* *Brit Med J* 1947, Oct 25, 641-5, 3 figs [22 refs]
- 11 BLACK, D A K & FOURMAN, L P R *Some Problems of Tropical Sprue* *Ibid* 645-7 [11 refs]
- 11 BRITISH MED J 1947, Oct 25, 660-61 [13 refs] *Fat Absorption and the Sprue Syndrome*

1 Steatorrhoea is observed in tropical and non-tropical sprue, coeliac disease, pancreatitis, gastro-colic fistula and other conditions. The process of fat absorption may be divided into an intraluminal phase (when it is prepared for absorption), an intracellular phase (in which the fatty material passes through the intestinal cell), and a distribution phase (when the fat is dispersed from the intestine by various pathways into the body).

*Intraluminal phase*—Fat is digested as triglyceride and there is no doubt that the fat is finely dispersed as an emulsion of particles less than  $0.5 \mu$  in the lumen of the small intestine.

In normal persons, the contents of the upper two-thirds of the intestine are acid (pH 6.5) and fat is absorbed in triple combination—fatty-acid-bile-salt-monoglyceride.

It may be concluded that long-chain triglycerides are partially hydrolysed in the upper part of the small intestine to fatty acids and lower glycerides, and that these two substances, with bile salts, provide the emulsifying system by which the remaining glycerides are dispersed into fine particles.

These changes normally occur in tropical and in non-tropical sprue and in regional ileitis, but not in conditions which interfere with any of the essential components of the emulsifying system.

*Intracellular phase of Fat Absorption*—Many water-soluble materials appear to pass through the outer membranes of the intestinal cell. Fatty acids pass into the intestinal cell possibly in the form of soaps.

Severe cases of sprue may show marked disturbance of water and electrolyte metabolism.

It has been suggested that adrenal cortical deficiency may be an aetiological factor in the sprue syndrome, but on the other hand, patients with non-tropical sprue can be relieved of any suggestive signs of adrenal insufficiency by appropriate treatment, without any change in the quantitative aspect of the fat-absorption defect.

Under special experimental circumstances, re-synthesis of triglyceride can be demonstrated *in vivo*. There is little evidence that it is an important feature in normal fat absorption. It seems possible that one important function of phosphorylation in the intestinal cell is to provide phospholipid for the change in interfacial film structure which must occur if the fat particles are to remain in a dispersed state in the protein environment of the bloodstream.

The author discusses the action of choline, and the theory that a defect in phosphorylation may be an aetiological factor in sprue.

Deficiencies of riboflavin or nicotinic acid are frequently associated with fat-absorption defects, especially the sprue syndrome. It is possible to obtain dramatic relief of signs and symptoms of deficiency by administration of the appropriate vitamins, without any measurable change in the fat absorption defect. A riboflavinosis and other vitamin deficiencies occur, in which fat-absorption is normal. It may be concluded that vitamin deficiencies, except, possibly, that of choline, are probably not concerned with the aetiology of fat-absorption in sprue.

*Distributive Phase of Fat Absorption*—Fat may be absorbed by at least two distinct mechanisms, each of which uses a different distributive pathway. The proportion of fat which is absorbed in particulate form may be reduced, with a corresponding increase in fatty acid absorption. The main factors which seem to be concerned in changes in the distributive phase apart from obstruction in the lymphatic pathway are the pH in the intestinal lumen and the composition of the dietary triglyceride.

ii. Neutral fat is absorbed as a very fine emulsion and when absorbed, enters the lacteals and alternately the systemic blood stream, when it may be visible as fine particles (chylomicrons). Split fat on the other hand, enters the portal system and may be absorbed without increasing the chylomicrons. In practical experience the authors have found the chylomicron count of limited value as a measure of fat absorption in view of the great variation in the size of the particles.

The authors used three methods of studying fat absorption in patients, namely chylomicron counts serum lipid curves and fat-balance experiments. As the result of experience they came to rely mostly on the last method. A significant difference was established between the fasting values in 9 normal persons and 16 patients with sprue in the latter the total fat was only slightly lower than normal after the meal, the increment in total fatty acid in those with sprue was only about half that in the normal persons but the normal range of fat curve was very wide, so that in the individual patient with sprue the curve might fall within the normal range. It was found that variation between successive four-day stool collections was very great, and in order to reduce error all results have been considered in twelve-day periods.

The excretion of fat can introduce only a small systematic error

Normal people taking a mixed diet containing 50 to 100 gm. of fat daily will absorb over 90 per cent. of it but in 28 patients with early tropical sprue fat absorption ranged from 50 to 85 per cent.

In therapeutic trials with nicotinic acid and riboflavin in large doses, no improvement in clinical state or fat-absorption was observed. Large doses of crude liver extract produced rapid clinical improvement but no detectable change in the percentage of fat absorption after several weeks, and thereafter only a slow improvement. 15-20 gm. of yeast extract daily however given to patients on liver treatment produced some improvement in fat-absorption in the first 1 days. Folic acid likewise may relieve all symptoms of the disease but does not increase the percentage of fat absorbed. Apart from glucose, the absorption of non-fatty substances in sprue has been little studied. If unabsorbed carbohydrates were as easily recognizable in the stools as are unabsorbed fats, the demonstration of impaired carbohydrate absorption in sprue might not have to be based on the equivocal evidence of blood-sugar curves which are so easily modified by non-absorptive factors. The evidence on this question is mostly indirect. Some general impairment of absorption was suggested by the finding that in the active stages of sprue the dry weight of the stools was increased to a greater extent than could be accounted for by their increased fat content. Iodide and amino-acids were abnormally absorbed. The evidence suggests that there is a fairly general impaired absorption in sprue and that fat malabsorption has been first observed only because its effects on the stools are more obvious.

*Salt deficiency*—In severe sprue the serum sodium and chloride were both found to be low. It was shown that large amounts of sodium and chloride were lost in the watery stools. Sodium was practically absent from the urine although chloride was still present in half the normal amount. This represents the biochemical pattern of salt deficiency accompanied by some acidosis.

Two findings are of practical therapeutic significance. Yeast extract in large doses exerts a favourable effect on fat-absorption. Secondly, a number of patients become acutely ill with salt deficiency dehydration associated with watery diarrhoea. In such patients, the diarrhoea must be controlled with sulphaguanidine and parenteral liver and the diet supplemented with moderate amounts of salt.

iii The editorial discusses the significance of these two papers and refers to other relevant work. It concludes that, "if our understanding of the physiology of fat absorption is imperfect, enough has been said to show that the absorptive defects in the sprue syndrome are even more mysterious." *P Manson-Bahr*

GELFAND, M. **Sprue and Coeliac Disease in Tropical Africa** *Trans Roy Soc Trop Med & Hyg* 1947, v 41, No 1, 109-18

The author has seen, and reports a case of, coeliac disease presenting the classical picture in an African child of 5, and he also reports a case of this condition in a European child of 2½ years. Both cases were rather milder in type than those encountered in Europe, and both did well under treatment.

It is generally held that tropical sprue is rare, if it occurs at all, in the dark-skinned races. The author has not seen this disease in an adult African. It is also said that sprue is rare in Europeans in Africa. Since 1941, the author has seen three elderly Europeans with incomplete sprue, in Rhodesia. All were originally diagnosed as suffering from malignant disease, in view of the wasting, all recovered on suitable dietary treatment.

Kwashiorkor (infantile pellagra) occurs in young children (1½ to 4 years) throughout most of tropical and subtropical Africa. The author considers the condition *not* primarily dietetic in origin for the following reasons—The onset is abrupt, in an apparently healthy child, the mother and other children in the family are usually well, the diets of the affected children appear to be adequate and kwashiorkor would not be so fatal if it were of nutritional origin, especially when it is diagnosed early and treated with an adequate diet. Suspecting that kwashiorkor might be due to jejunal deficiency, the author performed fat analyses on some cases, in some there was steatorrhoea, in others none, the results therefore do not support this thesis, or that kwashiorkor is a sprue-like disease. The author's belief is that it is primarily a liver disorder and at 3 autopsies he has observed a yellow fatty liver in each case. [Full data are given of examples of each type of case the author discusses.]

*A R D Adams*

SUAREZ, R M. El efecto de los conjugados de acido folico en el espru [Folic Acid Conjugates in Sprue] *Boletín Soc Med de Puerto Rico* 1947 Aug v 39, No 8 281-9

An account of 4 cases

## HAEMATOLOGY

COURDURIER, J & BRIGOO, E. Considerations sur la vitesse de sedimentation des hematies chez les Noirs en Afrique [The Blood Sedimentation Rate in Africans] *Méd Trop* Marseilles 1947, May-June, v 7, No 3, 254-9 [16 refs]

In the Hygiene Institute at Douala the authors studied the blood sedimentation rate in 50 healthy ex-service Africans from different parts of the Cameroons. Westergren's technique was used and tests were made each day

at the same time and under identical conditions. Readings were recorded after one and two hours. The average readings were 38.2 and 57.3 respectively but the variations were so great (0 to 137 for the first hour, 2 to 145 for the second) that these averages are of little value.

The authors discuss the various factors which might account for these high rates. While they were unable to disprove entirely any meteorological or racial influences, they do not consider that these were significant. Many parasitic infestations were found and these are discussed. The authors believe that these must be taken into account in assessing what constitutes a "normal" African—those in apparently good health, living with their parasites and living active lives would constitute normal people. The authors believe that the anomalies in the B.S.R., including the wide range of figures which made the establishment of an "average" reading impracticable, can be accounted for entirely by the high degree of parasitism encountered in apparently healthy Africans.

In the circumstances, the B.S.R., which is regarded as having a real value in Europe, cannot be considered of much assistance in French Equatorial Africa.

H. J. O'D. Burke-Gaffney

VAN UFFORD W. J. Q. Over de Bloedbezinkingsnelheid in de tropen. [Blood Sedimentation Rate in the Tropics.] *Ned. Maandblad*. Batavia. 1947 July No. 12, 220-22.

## VENOMS AND ANTIVENES

CHRISTENBERG P. A. & DE WAAL, Marn. Magnesium Sulphate and Carbolic Soap as Antidotes in Snake-Bite. *South African Med J* 1947 Sept. 27 v. 21 No. 18, 660-61

The good reports on the use of injections of magnesium sulphate solutions by SHIRCORE [this *Bulletin* 1947 v. 44 1017 and see also 1927 v. 24 800 and 1943 v. 40 625] and of 5 per cent. carbolic soap solution by ARUJA and BROOKS [ibid. 1946 v. 43 478] called for confirmation and both have been tested by the present authors in a properly controlled series of experiments. In the first, Shircore's method was followed closely. Dried venom of *Bitis arietans* was reconstituted in saline and 0.2 cc. (equivalent to 4-5 m.i.d. for guinea-pigs) was injected into the hind-leg muscles of each of 16 guinea-pigs and 5-10 minutes later 8 were infiltrated with local injections of 10 per cent. magnesium sulphate solution, the other 8 serving as controls. All 16 were dead within 3½ hours. The magnesium sulphate clearly was valueless against puff adder venom. Next, the protective value of the  $MgSO_4$  solution and of the soap were tested against the venoms of *Naja ferox* (the Cape Cobra), *Sepeiden hachmatters* (the ringhals) and *Bitis arietans* (the Puff Adder). The m.i.d. (0.06 mgm.) of the cobra venom was injected as before and 5 minutes later 9 guinea-pigs received 1 cc. of the sulphate solution, 9 the same amount of soap solution, 9 received 0.25 cc. antivenene and 9 were left as controls. With the *Sepeiden* venom the same method was used, but 0.5 ml. of antivenene—the *Bitis* venom was injected subcutaneously into the flank instead of intramuscularly because of the damage effected by the latter route, and 2 cc. of antivenene were injected. In a third test, the cobra venom was re-tested, with the use of 0.2 mgm. (or about 3 m.i.d.) and 40 animals were injected, 10 for each method of treatment and 10 untreated controls. The results are

presented in a detailed table, but they may be stated briefly thus the  $MgSO_4$  proved valueless, the carbolic soap solution was definitely protective against the cobra and the ringhals, useless against the puff-adder venom, it is to be recommended, therefore, as a first-aid treatment for cobra bites

H Harold Scott

DE MAGALHÃES, O O combate ao escorpionismo [Against Scorpions] Mem. Inst Oswaldo Cruz 1946, Sept, v 44, No 3, 425-39 [21 refs]

The question of dealing with scorpions is a serious one in parts of Brazil. Scorpion sting may be fatal even to adults, but even when it is not fatal it causes much pain, suffering and distress. In Belo Horizonte, 1,221 cases were recorded in 1941 and in three years 2,529, and, of course, many patients did not consult a medical man and so were not recorded. *Tityus serrulatus* seems to be the commonest and *T. bahiensis* next, but there are also two species of *Parabuthus*, *P. transvaalicus* and *P. triradulatus*, two of *Opisthophthalmus*, *O. wahlbergi* and *O. glabrifrons*, and *Hadogenes trogloditis dentatus*.

DDT, or Neocid in powder, is effectual in killing the scorpion after an interval, for treatment of stings, the appropriate serum given early is the best

H Harold Scott

MACCHIARELLO, A Cutaneous Arachnoidism or Gangrenous Spot of Chile. Puerto Rico J Pub Health & Trop Med 1947, June, v 22, No 4, 425-66, 5 figs [Refs in footnotes] [Spanish version 467-505]

The author presents a picture of the *mancha gangrenosa*, or gangrenous spot, of Chile. It results from the injection of a necrotizing poison by a spider, *Lorosceles laeta*. Clinically, arachnoidism in Chile may be divided into three groups: (1) Cutaneous, (2) viscerocutaneous, (3) nervous, the last due to the Black Widow spider, *Latrodectus mactans*.

Cutaneous arachnoidism is more common in the northern zone of Chile, from Antofagasta to Copiapó and Ovalle, rare, but not unknown, in the central area, cases are more often seen in the spring and summer, October-April, and more particularly January-April, but in some years no cases are seen. *Lorosceles laeta* is a house-spider, so most cases are "domestic accidents".

The symptoms of cutaneous arachnoidism, gangrenous spot, are nearly always purely local—sharp pain becoming a burning sensation, there are local oedema and erythema which spread, then the swelling hardens, darkens to violet or black by the third day, necrosis of the underlying tissue occurs (sometimes with a covering blister) and sloughing of a large surface up to 30 cm or even more in 2-3 weeks. There may be keloid development later. Strange as it may seem, apart from the first day's pain and insomnia, which are not relieved by morphia, there are no constitutional symptoms. Details of 25 cases illustrating the above are given.

In the viscerocutaneous form, the same spider is the cause and the reason for the production of generalized symptoms (such cases are few) is thought to be the injection of the poison directly into some vessel of the skin. In these patients there are rise of temperature, haematuria, jaundice, asthenia and vomiting. Red corpuscles are reduced by some 60 per cent whereas the leucocytes are increased to about the same degree. Differentially, the chief change is an increase in large monocytes at the expense of the polymorphonuclears.

Study of the poison shows that it is not of itself haemolytic and the pathogenesis of the haematuria awaits explanation. The difference from the bites

of *Lairodectus mactans* rests in the absence of general symptoms and the localized coagulant and necrotic action, whereas *L. mactans* has a special action on the nervous system and the symptoms are generalized. H. Harold Scott

## DERMATOLOGY AND FUNGUS DISEASES

DORMER, B. A. & SCHER, P. Case Report X. Tumor of the Lung due to *Cryptococcus histolyticus*. Clin. Proc. Cape Town. 1947 Aug v 8, No. 8, 289-73 6 figs.

NEGROMI, P. FERNÁNDEZ L. L. & DAGLIO C. A. N. A propósito de un caso de pie de Madura con gránulos negros. Revisión de los micetomas producidos por "Madurella" [Concerning a Case of Madura Foot with Black Grains. Review of the Mycetomas caused by *Madurella*.] *Rev. Argentina Dermatología*. 1947 June v 31 No. 2 192-205 3 figs. [34 refs.] English summary (8 lines)

The authors present a review of the history and nomenclature of the species of the genus *Madurella* Laveran and supplement this with an analytical table of the reported characters of the fungi. They also describe the fungus from a case of black grain mycetoma from Argentina, which they have identified as *Madurella ramiroi* da Silva. A fungus from the same lesion had previously been diagnosed as *Aspergillus chevaleri* by two other pathologists.

[The time is ripe for a revision of the species of *Madurella* some of which are based on a study which did not include the examination of the fungus in saprophytic culture and there is little doubt that several of the specific names should be treated as synonyms of *Madurella mycetozoa*.] J. T. Duncan

DE ALMEIDA, F. RIBEIRO D. O. ASHCAR, H., LACAZ, C. da S. & SAMPAIO, S. de A. P. I. Ação da penicilina, in vitro sobre o paracoccidioides brasiliensis. II. Resultados obtidos com a administração desse antibiótico no tratamento da blastomycose sul-americana. I. Action of Penicillin on Cultures of *Paracoccidioides brasiliensis*. II. Results of Administration of Penicillin to Patients suffering from South-American Blastomycosis.] *Hospital*. Rio de Janeiro. 1946, Jan., v 29 No. 1 181-4 1 fig

I. Reports on the action of penicillin on mycotic fungi have been discordant the studies of KRENEY AJELLO and LAMFORD (*Bull. Johns Hopkins Hosp.* 1944 v 75 410) led them to conclude that The use of penicillin in the treatment of the superficial and the deep mycotic infections is unwarranted and contra-indicated. The present authors, nevertheless, resolved to test its effect on cultures of *Paracoccidioides brasiliensis*. In each of four tubes of Sabouraud broth, pH 8-4 they placed a fragment of the culture obtained on solid Sabouraud glucose. The tubes were then incubated at temperatures ranging from 24 to 48°C. and when growth appeared, there were added daily 1 the first three tubes 1 10 and 50 Oxford units of penicillin respectively the fourth being left as control. Five days later examination revealed that in tube 1 there were more than 32 units, in tube 2 more than 32 and in tube 3 more than 100 units. In spite of continuing the daily addition of penicillin, at the end of ten days the growth in all the tubes was the same. Photographs of the tubes are reproduced in the article.

II. Penicillin was given to each of three patients suffering from different forms of South American blastomycosis. The first with the glandular form,

was given 20,000 Oxford units of sodium penicillin intramuscularly every 3 hours. After a total of 600,000 units had been given, treatment had to be suspended because the patient seemed to be "physically worse". The second, with the cutaneous and glandular form, was given 25,000 units every 3 hours intramuscularly, to a total of 1,300,000 units. The third, with the mucous membrane form, was given 50,000 units in the same way to a total of 3,000,000 units. In all three there was observed at first a slight improvement in the cutaneous and mucous lesions, they were softer and less oedematous, but no further amelioration took place. The early improvement is ascribed to the effect of the penicillin on the secondary infections. In short, in the doses given, the penicillin was without action on the blastomycotic condition.

H. Harold Scott

CAMPOURCY A. Chromoblastomycose au Cameroun [Chromoblastomycosis in the Cameroons] *Bull Soc Path Exot* 1947, v 40, Nos 7/8 252-3, 1 fig

HABIBI, M. *Rhinosporidium seeberi* en Iran [*Rhinosporidium seeberi* in Iran] *Ann Parasit Humaine et Comparée* 1947, v 22, Nos 1/2, 84-8, 4 figs

Rhinosporidiosis, caused by *Rhinosporidium seeberi*, is a relatively rare mycosis, the total number of reported cases, from all countries, does not exceed 165. Habibi has observed 31 cases in Persia since 1937, before that date the disease had not been recognized in the country.

An analysis of the age incidence in 28 of the Persian cases shows that 10 contracted the infection between the 10th and 20th years, 7 between the 20th and 30th years and 4, 3, 2 and 1 in each of the succeeding decades. Only one patient was under 10 years of age. The disease is not associated with any particular occupation, but the highest number of cases occurred amongst scholars, which may be related to their ages or to the greater possibility of transmission of the infection during play. Geographically, 16 of the cases were connected with Ardebile, 13 with Teheran and 1 each with Ispahan and Kermansha. In 22 cases the polyp arose from the nasal mucosa, in 7 from the conjunctiva of the eye or eyelid and in 2 from both nose and eye. In treatment, strangulation of the polyp at its pedicle with a silk ligature, as practised in the Ardebile district, gives only transient relief followed by recurrence, instillation of a weak solution of tartar emetic, advocated by WRIGHT, proved ineffective, but electro-coagulation of the polyp and its immediate neighbourhood, or surgical excision followed by cauterization of the base of the tumour, gave the most satisfactory results.

J. T. Duncan

LANGERON, M. *Trithrachium brumpti* (Langeron et Lichaa 1934) Langeron 1947 et le genre *Trithrachium* Lumber 1940 [*Trithrachium brumpti* and the Genus *Trithrachium*.] *Ann Parasit Humaine et Comparée* 1947, v 22, Nos 1/2, 94-9, 1 pl & 1 fig [13 refs]

The fungus described from a case of ocular mycosis in Egypt as *Beauveria brumpti* [this *Bulletin*, 1935, v 32, 898] is here re-named *Trithrachium brumpti* and four other fungi found associated with disease in man are also transferred to the latter genus. The pathogenicity of these five species of *Trithrachium*, which are, in the author's opinion normally saprophytes of world-wide distribution appears to be weak.

G. C. Ainsworth

## HEAT STROKE AND ALLIED CONDITIONS

CONSOLAZIO, W. V., PECORA, L. J. & TURNING, T. A Slow Dissolving, Non-Irritating Salt Tablet for Use in Hot Environments. *J. Indust. Hyg. & Toxicol.* 1947 Sept., v 29 No. 5 347-50 2 figs.

Severe symptoms of nausea, vomiting and epigastric discomfort are frequent as a result of the use of ordinary salt tablets to combat the effects of heat and excessive sweating. It was believed at first that these symptoms were due to prolonged contact of the salt with the gastro-intestinal mucosa. Salt tablets prepared with cornstarch to bring about rapid solution were, however, not satisfactory. Slowly dissolving tablets were then prepared on the assumption that with these the salt concentration might never be great enough to cause irritation of the mucosa. These tablets were found to be very satisfactory in a number of trials.

These slowly dissolving tablets are prepared by treating ordinary salt tablets with a solution of cellulose nitrate or acetate and then drying at 100°C. to remove the solvent. This procedure gives rise to the formation of a honeycomb structure. The impregnating film of cellulose weighs about 4 mgm. per tablet of 0.65 gm. In a few experiments no evidence was found of any toxic effects in animals through the ingestion of cellulose nitrate or acetate. The solution time of the impregnated tablet is of the order of eighty minutes compared with fifteen minutes for the pure salt tablet and one minute for the salt-cornstarch tablet.

M. E. Delefield

## TROPICAL ULCER

LICHTMAN, J. A. Tropical Ulcer with special reference to its Etiology. *Chz. Proc. Cape Town.* 1947 July v 6, No. 5 165-80, 14 figs. & 3 charts. [72 refs.]

This paper is based on the personal study of 180 patients treated in Durban, Natal.

It is usually agreed that tropical ulcer may start as —

- (a) infection of a wound or other lesion (most commonly)
- (b) spontaneously as a vesicle which bursts in a few days (probably uncommon.)

*Site.*—The author in his series found that 41.4 per cent. of ulcers occurred on the anterior surface of the leg in its middle or lower thirds and rarely occurred elsewhere than on the lower extremities (all observers are probably agreed on this). An adherent yellowish-grey slough at the base of the ulcer was a characteristic feature and pain was a frequent symptom. The chief complication was extension especially in depth and in 34 per cent. of cases the ulcer had extended to tendon and bone. Spontaneous fracture of underlying bone has been recorded.]

Surrounding multiple ulcers indicative of auto-inoculation were not uncommon, but lymph-spread was not a feature and no cases of malignant change were found in this series (VITT in Kenya found microscopic malignant changes in 2 per cent. of cases examined). Scars of previous ulcers were found in 43 per cent. which does not support the theory that one ulcer confers immunity.

*Bacteriology.*—Fusiform bacilli were found in 70 per cent. spirochaetes in 60 per cent. but these were always found together with fusiform bacilli. In only 36.6 per cent. were fusiform bacilli and spirochaetes found without other



# Miscellaneous Diseases

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organisms Although other organisms such as Gram-positive diplococci, staphylococci and streptococci were met frequently, the predominating ones were fusiform bacilli and spirochaetes

Diphtheria and diphtheroids were uniformly absent, streptococci were not conspicuous, Leishman-Donovan bodies were not found, either in smears or sections, blastomycosis, actinomycosis, and evidence of other mycotic organisms were not found

The fusiform bacilli and spirochaetes were morphologically identical with those of Vincent's angina, and the author considers that they are causal and pathogenic for the following reasons —

- 1 In 36.6 per cent they were the only organisms found in active lesions,
- 2 They are associated with a definite clinical type and can invade living tissue,
- 3 Tropical ulcer has been reproduced in human beings with pure cultures of fusiform bacilli by intradermal injection plus some form of trauma [see this Bulletin, 1946, v 43, 378]

Trauma undoubtedly plays a large part in causation, and contact with saliva (in which fuso-spirochaetes are often present) is a likely mode of infection

*Climate* — Cases are very rare outside the latitudes 35°N and 10°S, although the author's series come from Durban, 30°S Local predisposing causes are probably increased liability to injury due to scanty clothing in hot climates and increased skin moisture predisposing to bacterial growth [cf prickly heat]

The author was unable to incriminate syphilis, malaria, hookworm, bilharzia or anaemia as important predisposing causes, although he does consider that in West Africa sickle cell anaemia may play a part

*Dietary deficiency* is undoubtedly a predisposing factor Thus meat- and fish-eating tribes are much more rarely affected than those whose diet is mainly vegetarian and where the protein is of low biological value [cf the rarity of this condition amongst the Masai, who live mainly on meat, milk, and blood, despite the fact that they live under very dirty conditions and are very prone to injuries of the lower extremities] The author was unable to find evidence of deficient protein content in the serum of ten consecutive unselected cases but he does consider vitamin deficiency, especially lack of nicotinic acid or of flavin, to be an important predisposing cause, he notes the prevalence of "crazy pavement" skin and pigmentation of the legs

*Local predisposing causes* — Dirt and exposure to injury are regarded as important, but the presence of peripheral neuritis was not noted The preface contains several tables and some excellent photographs

C F Shell

## MISCELLANEOUS DISEASES

CHODZKO, W Persistent Endemic Foel of certain Acute Infectious Conditions Remarks on their Extinction Bull Office Internat d'Hyg Publique 1946, Oct-Nov-Dec, v 38, Nos 10-11-12, 913-34 [40 refs] [French version 889-912, 3 maps]

The Polish delegate's report to the Permanent Committee ranges over many diseases and presents again many facts and ideas of interest It is worth remembering that Ferran was early in the field, possibly the first in the world with vaccination against cholera in Spain and his vaccine was, like the fixed antirabic virus of Pasteur, a vaccine of living organisms Mention is made by Chodzko of Rogers' denial that cholera spreads throughout India from Bengal [One wonders whether an endemic home for cholera, usually allotted to India

and China, might not be found in the valley of the Russian Don?] Influenza is given its original endemic centre in China, especially in the basin of the Yellow River of North China. An interesting point is made of a frequent association, which manifested itself in Poland after the first world war — epidemic relapsing fever nearly always follows epidemic typhus fever. The phenomenon, which is probably not accidental although the former is a spirochaetosis and the latter a rickettsiosis, also occurred in Algeria, Egypt and Roumania following the first and second world wars. Whenever there is a big world-wide conflagration, the hideous face of louse-borne typhus fever appears on the scene. References are made to the tick-borne and mite-borne typhus fevers and to the great danger of aeroplane introduction of the disease to the prophylactic vaccines that are now available of which the first in order of discovery was the Polish vaccine of Weigl to DDT insecticide and to the Soviet antiseptic soap. Plague although said to have its original endemic centre in central Asia has, at various times swept over Europe. Sylvatic epizootic plague has, perhaps, received more attention of recent years than epidemic plague. The possibility that plague-infected fleas may travel even by ship hidden in bales of jute to start the disease in a distant country is mentioned — this subject has received recent attention. Smallpox, like those diseases already mentioned receives a special heading and special commentary. In Russia, vaccination against smallpox started to be carried out in 1803 but it was not until 1909 that vaccinations and revaccinations were made compulsory by a special law which was followed by striking success. Poland freed itself from smallpox in 1919 and since 1906 not a single case of smallpox has been notified.

There is again a special commentary on giardiasis as presenting a special pandemic problem. The author reminds us that the causal agent of the disease, originally known as *Lamblia* owes its name to Professor Lambl, a Czech scientist, and professor of medicine at Warsaw University. The professor himself called the parasite *Cercomonas*. As there are large numbers of carriers of the organism it would appear necessary to introduce compulsory notification of cases of giardiasis which is a real triable pandemic disease.

W. F. Harvey

ASH, J. E. The Lymph Node in Tropical Diseases. *Amer J Trop Med* 1947 July v 27 No. 4 483-91 10 figs.

In lymphopathus venereum (climatic or tropical bubo) the stellate abscess cannot be differentiated from the granuloma of several other infections, particularly tularemia. It is closely simulated in filarial infection, but is readily distinguishable from that of tuberculosis and syphilis by the type of necrosis.

In scrub typhus, there is generalized adenitis and the glands may show areas of gross necrosis. In Oroya fever the lymph nodes are specifically concerned, because of the involvement of the reticulo-endothelial system. A less specific feature is sinus catarrh. The sinuses are dilated, the endothelium swollen and the lumina filled with lymphocytes and large macrophages.

In yaws, the treponemata are demonstrable, in the lymph nodes.

The reaction of the lymphatic tissue to *Brucella* bears a considerable similarity to that of Hodgkin's disease. Most pathologists have recognized in brucellosis a non-specific and non-neoplastic reaction—such as is seen after irradiation, and which was observed especially in the testes of Japanese atomic-bomb victims. In *Brucella* infections, especially of *Br. melitensis* origin, it is seen more particularly in the mesenteric glands and spleen, and includes the presence of multinucleated cells indistinguishable from the Reed-Sternberg cell of Hodgkin's disease.

Typhoid fever is a lymphadenotropic infection with a reaction that is usually characteristic enough to warrant identification in absence of other criteria. The typhoid cell is a large mononuclear cell which tends to collect in foci and displace the normal lymphatic tissue.

In all cases of plague, there is localization of *Pasteurella* in the lymph nodes. The primary localization of the organism is there. The toxin of *P. pestis* causes necrosis of the vessel walls, and the reaction is characterized by extensive necrosis and haemorrhage.

In leprosy, involvement of the lymph nodes is a constant feature, so that diagnosis may be made bacteriologically by aspiration of the inguinal glands. In the early stages, pigmented foam cells are scattered near the cortex and contain bacilli. Histoplasmosis is the only fungous disease with a predilection for the reticulo-endothelial system.

In leishmaniasis the lymph node is not particularly involved, except in heavy infections. The glandular lesions of filariasis (*W. bancrofti*) infections are too well known to need further description. *W. malayi* may localize about the mammary gland or in the axilla. An interesting feature of the histology is that eosinophils may be present in lymph nodes in which these worms may not necessarily be identified. *P. Manson-Bahr*

SCHWETZ, J. Sur la rivière Fwa (Congo belge). Notes géographiques, zoologiques et médicales [Geographical, Zoological and Medical Notes on the River Fwa, Belgian Congo]. *Inst Roy Coloniale Belge—Bull des Seances* 1947, v 18, No 1, 271-95, 1 text fig, 5 figs on 2 pls & 1 folding map.

"Lake Fwa" in the Belgian Congo is 155 km from Lusambo and 135 km from Luluabourg. Its natural beauty attracted many tourists and a small hotel was built on its banks. Soon after a large proportion of visitors were infected with schistosomiasis, a large number of lakeside native dwellers were likewise found to be infected. The hotel was closed, European visitors ceased to visit the lake, fishing was prohibited, and the villages were removed to a distance from the banks. The author of this report spent twelve days at Fwa and gives the results of his observations.

"Lake Fwa" is not a lake, but a river of an unusual kind. Gushing springs emit such large quantities of water that the resulting river is very many metres wide near its source. The river flows 15 km to join the river Lubi, its width varies from 50 to 200 metres or more.

The author writes enthusiastically of the natural beauties, the fish and birds. Mosquitoes were very abundant. Of 722 specimens identified there were 601 *A. funestus*, 99 *A. marshalli* var *moucheti* and 22 *A. gambiae*. Larvae of three other anophelines were found, *A. constanti*, *A. paludis* and *A. obscurus*. *Phlebotomus* and *Culicoides* were very abundant, *P. africanus*, *P. schwetzi*, *P. decipiens* and *Culicoides mornati* pennis. *Glossina palpalis* was found, but was not abundant along the river banks.

The molluscan fauna was rich. 11 species were found. 10 Gasteropods and 1 *Lamellibranch*. There were two species of *Planorbis*. *Biomphalaria adovensis* and *Hydrobia orbis salinarum*.

An examination of 70 villagers in one nearby village revealed 21 with schistosomiasis, 45 with ankylostomiasis and 28 with ascariasis. *Norman White*

DE ALBUQUERQUE, A. F. R. & MACHADO, A. C. Contribuição ao conhecimento da nosologia de Alagoas [Disease in Alagoas]. *Rev Hig e Saude Publica* 1947, Apr-June, v 5, No 1, 21-34, 2 maps.

Alagoas occupies an area of 28 571 kilometres between 8°55' and 10°28' south latitude and 5°15' and 5°10' east longitude of the meridian of Rio de Janeiro.

After a brief account of its physiogeography, the authors consider three diseases and their vectors, viz., the Triatomidae, yaws and schistosomiasis.

Of 2,338 Triatomidae examined, 2,328 (99.5 per cent.) were *Paratrypanozoa megistis* and 410 (17.6 per cent.) were infected with *T. cruzi*. 7 were *Eutritomus maculata*, one infected and 5 were *T. brasiliensis* 2 infected. A table gives the distribution of *P. megistis* in 23 localities—most, in actual numbers and percentage, were in the wooded districts.

Yaws was systematically taken in hand in 1943—treatment units being established. In 17 of the 33 municipalities the numbers recorded for the three years 1943–45 were, respectively, 1,883, 3,323 and 4,623—the numbers in the different municipalities are shown in a table [but this would be of local interest only].

Schistosomiasis mansoni is common in the wooded and maritime regions—the snail hosts are *Australorbis centumtralis* and *A. obsoletus*. Another mollusc, of the genus *Ampullaria*, abounds in the State—one of these was found parasitized by a locked cercaria in 1943. Ten localities are detailed in a table. In Macisé of 13,098 persons examined, 863 (5.8 per cent.) were positive—among 2,646 children in schools in the same district 59 (2.2) were positive—among 2,341 in the Rio Largo district 738 (31.5) were infected. In other places the percentages positive were high—but the numbers examined were small.

H. Harold Scott

GALLO P. & VOGELBEIN E. G. Las zoonosis en Venezuela. [Diseases of Animals in Venezuela.] VII Conferencia Sanitaria Panamericana. Cuadernos Amarillos. Publicaciones de la Comisión Organizadora, No 27. Caracas, 1946, 53 pp. [Bibliography.]

An interesting article, not confined to veterinary diseases, as the title would imply—but a consideration of the diseases common to animals and man, or communicable from animals to man. All the usual diseases are mentioned—rabies, encephalo-mylitis, anthrax, parasitic infestations, etc. One section of particular interest is that dealing with animals which act as reservoirs of human disease in Venezuela, as howler monkeys and yellow fever rats and plague, canine and human leishmaniasis, opossums and armadillos and Chagas's disease, dogs and *Demodex* and human rabies.

H. Harold Scott

DEMAN K. Jean-Marie. Un myriapode chélopode *Orphnus brasiliensis nigropictus* Att. de l'oreille humaine en Equateur. [A Myriapod, *Orphnus brasiliensis nigropictus* Att. from the Human Ear in Ecuador.] Ann. Parasit. Humain et Comparé 1947 v. 22, No. 1/2, 63–7, 6 figs.

## PROTOZOOLOGY GENERAL

WENRICH, D. H. The Species of *Trichomonas* in Man. J. Parasitology 1947 June, v. 33 No. 3 177–83, 3 figs. [Numerous refs.]

The author returns to the subject of the species of *Trichomonas* in man which he previously discussed (this Bulletin 1944 v. 41 607). He gives further details for their differentiation and discusses the relevant literature. He concludes that the oral form (*T. tenax*) and the vaginal form (*T. vaginalis*) with four anterior flagella are closely related, while the intestinal form (*T. hominis*) possesses five anterior flagella, four of which arise from a single blepharoplast as do the four flagella of *T. tenax* and *T. vaginalis* while the fifth originates in a single small ventral blepharoplast. The author is careful to note that *T. hominis* is the only intestinal form he has seen, but admits that forms with three and four flagella may occur. The paper is illustrated by three diagrams showing the structure of the three species discussed.

C. M. Hennyow

KIRBY, H. Flagellate and Host Relationships of *Trichomonad* Flagellates *J Parasitology* 1947, June, v 33, No 3, 214-28 [40 refs]

The author discusses the flagellates of the genus *Trichomonas* and other flagellates that have basic features of structure and a type of cell division comparable to that of *Trichomonas*. Many of the forms considered are parasites of termites. C. M. Wenyon

CROSS, JOY B. A Cytologic Study of *Toxoplasma* with special reference to its Effects on the Host's Cell *J Infect Dis* 1947, May-June, v 80, No 3, 278-96, 52 figs on 4 pls [Numerous refs]

The author has studied the morphology of toxoplasma as exhibited by two strains maintained in mice. Material from the peritoneum was used and fixation was always by the wet method—Bouin's solution, Flemming's fluid, Schaudinn's fluid, and 10 per cent formalin. For staining, various methods were adopted, including Feulgen reaction. It is pointed out that in the peritoneal cavity the parasites are both extra- and intra-cellular and when in the latter situation, in spite of their multiplication, they do not interfere with the nuclear division of the host cell. The parasite contains a shadowy band of cytoplasm which divides it longitudinally. This is termed the "cytostyle". Another structure which is occasionally seen is a phlange which stretches from one end of the parasite to the other. It is assumed that the appearance of the parasite as a crescent in dried films is due to the failure of this phlange to stain. Apart from the nucleus a number of granules are present in the cytoplasm. The nucleus is described as dividing by mitosis with persistence of the nuclear membrane. This is specially clear in specimens stained by Feulgen's method. Reproduction is by binary fission, there being no evidence of any schizogonic process. Eventually the intra-cellular parasites are so numerous that the host cell nucleus is extruded, leaving a terminal colony of parasites surrounded by a membrane representing the remains of the host cell. From her observations, the author concludes that the parasite is a protozoon. In three slides, some 50 flagellated organisms were encountered but the author is uncertain as to their identity. The paper is illustrated by a number of drawings.

[It is perhaps unfortunate that no mention is made of the living organisms as these might have served as controls of the fixed specimens, many of which appear to the reviewer to be abnormalities. In fixed specimens, the prevailing type of nucleus is that of a vesicle with small central karyosome.]

C. M. Wenyon

## ENTOMOLOGY AND INSECTICIDES GENERAL

HILL, Marjorie A. The Life-Cycle and Habits of *Culicoides impunctatus* Goetghebuer and *Culicoides obsoletus* Meigen, together with some Observations on the Life-Cycle of *Culicoides odibilis* Austen, *Culicoides pallidicornis* Kieffer, *Culicoides cubitalis* Edwards and *Culicoides chiopterus* Meigen. *Ann Trop Med & Parasit* 1947, May, v 41, No 1, 55-115, 12 text figs, 5 figs on 2 pls, 6 graphs & 2 histograms [75 refs]

The primary object of these investigations was to fill in the gaps in our knowledge of the life cycle of *Culicoides impunctatus* and *C. obsoletus*, the most wide-spread and annoying "midges" in Britain.

The paper contains detailed records of twelve months' work in the neighbourhood of Liverpool during 1945-46. It includes a very full survey of the literature on the genus, dealing with the life-cycle, the morphology, British species and laboratory technique.

After describing the site of the investigations, the type of soil, the flora in different plots of ground and the methods and materials employed, the author discusses the experiments made and the conclusions drawn from them. An illustrated account is given of the morphology of all stages of the different species. Data from the experiments are presented in full.

For the collection of adults, netting, light traps and human baits were first employed but were later abandoned. Daily collections were made in the summer of 1945 before sunset each evening as the insects alighted on a black cloth suspended above the ground. Adults were bred in the laboratory in lamp chimneys and feeding was first done on the sorter's arm but later on the shaved ear of a rabbit. Rearing was done in earthenware pots covered with lamp chimneys having organdie fastened over their narrow ends. The medium for *C. impunctatus* was peaty soil and for *C. obsolatus* decaying leaves and mud. Some were kept at 22° to 24°C. but the majority were reared at laboratory temperatures of 16° to 19°C.

From the results of the field and laboratory experiments it was concluded that *C. impunctatus* has a marked preference for human blood. This species was the commonest in the locality and there seems to be one generation per year with a peak in June. Adults began to appear in April and the last were caught in August. They were most active from half an hour before sunset through the night to early morning and did not travel far from their breeding places. Fourth stage larvae were found from November to July, and pupae from April to July. Laboratory studies indicated that the eggs take two weeks to hatch, the larval stage lasts about five months (though some larvae may take as many as seven) and the pupal stage takes 5 days.

*C. obsolatus* appeared to feed more readily on rabbit's blood than did *C. impunctatus*. There seem to be two generations in a year with peaks in June and September. Eggs hatched within 3 days of laying, the larval stages lasted 3½ to 5 months and the pupal stage 5 days. The life cycle of a strain of this species reared in the field occupied six months in the summer and nine months during the winter.

The more limited observations on the other species indicate that they have but one generation in a year.

H. S. LEWIS

HILL, Marjorie A. & ROBERTS, ERIC W. An Investigation into the Effects of "Gammexane" on the Larvae, Pupae and Adults of *Culex impunctatus* Goetghebuer and on the Adults of *Culex obsolatus* Meigen. *Ann. Trop. Med. & Parasit.* 1947 May. 41 No. 1 143-63 8 graphs. [10 refs.]

The experiments recorded in this paper were made in Knowsley Park, Liverpool, in the summer of 1946. For the experiments on the immature stages, three sites were chosen in damp soil rich with humus, half shaded by rhododendron bushes. Sampling showed that each site contained a similar proportion of larvae and pupae and that they were present only in shaded portions, also that pupation commenced in May. The three plots were sprayed once, in May, one with 5 per cent. Gammexane in miscible oil plus lake water at 100 mgm. Gammexane per square foot, one with lake water only, and the other with miscible oil plus lake water.

Field tests showed no larvae or pupae in the Gammexane plot after thirteen days. In the control plots, the number of immature stages increased after the twentieth day until the seventy-seventh day (though there were no pupae after the forty-third day) after the seventy-seventh day the number of larvae decreased until the 126th day, the last of the experiment. No pupae from the "Gammexane" plot produced adults, but those from the controls produced 100 per cent. adults.

Laboratory tests of residual toxicity of soil samples from the 'Gammexane plot' showed a continuous increase in the time required to give a 100 per cent kill of larvae. In the first fortnight, twenty-four hours immersion was sufficient, but after the seventeenth week seven days' contact with the sample of treated soil was necessary to kill all larvae.

Soil penetration tests showed that Gammexane was present in a toxic concentration at a depth of one centimetre during dry weather, but effective penetration was increased to three centimetres after heavy rain and toxicity was still maintained even when the ground was water logged. However, toxic effects were never observed to extend to a greater depth than three centimetres.

Observations suggest that Gammexane on the soil surface has but a limited effect on ovipositing females and it is uncertain whether Gammexane exerts any ovicidal action or whether it kills young larvae as they hatch from the eggs. From the experiments with early stages, it is concluded that spraying the breeding places with 5 per cent Gammexane at 100 mgm per square foot in May not only destroys the generation of *Culicoides* about to emerge, but also prevents development of adults in the following summer.

In the tests against adults of *Culicoides* five black cloths, each  $1\frac{1}{2} \times 2$  feet, were saturated with 75, 150, 300, 600 and 1 500 mgm of Gammexane in benzene to give deposits of 12.5, 25, 50, 100 and 250 mgm per square foot respectively, one other cloth was soaked in benzene only. The cloths were suspended 4 to 5 feet from the ground and left exposed for a month. Flighting midges were collected the first evening, starting one hour before sunset, and ten minutes were allowed for each cloth. Other evening collections were made on four occasions at intervals of six days.

It is shown that the cloth with the highest concentration of insecticide was effective in killing all flighting midges for one week, other treated cloths were less efficient. Toxicity was lost at a steady rate on all cloths, until by the third week it was negligible. It is therefore concluded that this method is not likely to prove satisfactory in the control of adult *Culicoides* except for about two weeks in a restricted area.

H. S. TILSON

DE MEILLOU, B. & GEAR, J. A Note on Three Noxious Arthropods occurring on the Wiltwatersrand. *South African Med. J.* 1947, June 14, v 21, No 11, 107-11, 3 figs.

The "Black Widow Spider" *Latrodectus* is found in many areas in Rhodesia and South Africa. Two species, *L. geometricus* and *L. indistinctus* are found. This paper gives some account of the appearance and habits of these spiders, and case records of two severe instances of spider bite are described. Fatalities have occurred and the case mortality rate is approximately five per cent.

This paper also contains an account of the "Tumbu Fly" *Cordylobia anthropophaga*, descriptions of which will be found elsewhere, and also of the plant sucking bug *Piratus lugubris* which sometimes gives a painful bite, although it does not feed on mammals.

Kenneth Mellanby

OLDROYD, H. Notes on the Type-Specimens of African Tabanidae (Diptera) described by Mr H. F. Cartor (1912, 1915). *Ann. Trop. Med. & Parasit.* 1947, Sept. v 41, No 2, 234-8, 1 fig.

WOKE, P. A. Arthropods of Sanitary Importance in the Republic of Nicaragua, Central America. *Amer. J. Trop. Med.* 1947, May, v 27, No 3, 357-75, 1 map.

A list of arthropods collected during brief visits to Nicaragua. It is very incomplete, but as the fauna of this country is imperfectly known, it may be of some value.

Kenneth Mellanby

JENNINGS, D. W. A Laboratory Method of rearing Chiggers affecting Man (Acarina: Trombididae). Reprinted from *Ann. Entom. Soc. America*, 1947 Mar v 40 No 1 56-68, 4 pls. [10 refs.]

The author describes his successful experiments in rearing the North American species of *Trombidula*. He reviews earlier work, from which it appears that even the most successful experimenters could only maintain these mites for one generation and with a high mortality.

Three species are known to occur in the United States *Eutrombidula alfredugei masoni* and *batatas* (? *housmanii*) of these the last is confined to the southern States and also occurs in Tropical America. The author generally started his breeding by putting down black cards and collecting unengorged larvae which walked on to them or he collected wild reptiles which were generally infested and allowed engorged larvae to drop off them. He found that under laboratory conditions larvae of the three species very readily attached themselves to snakes, lizards or turtles (*Terrapene*). The last-named are found to be the most convenient to handle. He also recovered wild larvae by staking out a turtle in a suitable place for a few hours.

In rearing the stages which occur in soil it is necessary to work at high humidity but to avoid condensation in which larvae may be drowned. It was found convenient to use a jam jar with the bottom removed and a plug of plaster of paris put in in its place. The jar was closed by a screw top through which the larvae did not escape a hole was drilled in it and plugged with wool. The actual rearing medium was either sterilized humus or loose sandy soil.

In these containers, nymphs and adults fed on eggs of *Aedes*. If the shell of the egg is moistened, the mite can pierce it and remove the contents in a few minutes. This is clearly an unnatural food, but the extreme neatness with which the mite carries out this task might suggest that eggs of some other insect are a normal food. The mites ate such large numbers of eggs that it was found very difficult to provide enough for the purpose. It seems that the female mites lay an average of about ten eggs per day much higher figure than had been expected. The reproductive potential must be high, for the author obtained about 6 000 larvae during two months from a culture containing twenty-three females. The minimum time under which the life-cycle was completed was 50 to 70 days.

The paper contains a large amount of valuable detail. It is clear that the author has maintained these mites for several generations and produced very large numbers of larvae for experimental work. His methods have greatly reduced the amount of handling required and it seems that the mortality was low.

P. A. Buxton

GOODWIN, R. L. Evaluation of Pyrophyllite as an Insecticide Diluent. *J. Econom. Entom.* 1947 Apr v 40 No. 2, 270-73 3 figs.

Pyrophyllite is hydrous aluminum silicate  $H_2O \cdot Al_2O_3 \cdot 4SiO_2$  formed by hydrothermic alteration of volcanic deposits. It is rather difficult to distinguish from talc (the molecules of which are similar but with 3 atoms of magnesium substituted for two of aluminum) except by the mineralogist's blowpipe test with the use of cobalt nitrate solution.

Pyrophyllite is widely used as a diluent for insecticides in powder form, but there is some controversy about its merits. Three points are important in this connexion —

- (1) Various other minerals are sometimes sold as substitutes (e.g. mica)
- (2) It is easily confused with talc.
- (3) Quartz is sometimes present as an impurity to the extent even of 25 to 30 per cent. This causes an abrasive effect which may have important bearing



on the insecticidal action of a mixed dust. Other dusts used as diluents (e.g. talc or kaolin) also may contain quartz and it is important to consider this in making comparisons between these diluents

J R Busvine

GARNHAM, P C C **Mortality of *Aedes aegypti* feeding on Rabbits receiving Oral "Gammexane"** [Correspondence] *Nature* 1947, Aug 2, 156-7.

Previous workers have shown that insects may be killed by taking the blood of a mammal fed with DDT (LINDQUIST *et al.*, *J Econom Entom*, 1944, v 37, 128) or Gammexane [DE MEILLON, this *Bulletin*, 1947, v 44, 469]. The present investigation used *Aedes* mosquitoes to determine how long the lethal effect lasted, and the minimum effective doses.

It was found that single doses of 40 mgm per kgm of Gammexane given to rabbits killed all *Aedes aegypti* subsequently feeding on them for about four days. Lower doses were sometimes ineffective shortly after they were given to the rabbits, but later were insecticidal. [This suggests that the concentration of Gammexane in the blood rose, up to twenty-four hours after it was swallowed.] These lower doses were insecticidal for about two days only. It was not feasible to go above doses of 40 mgm per kgm which caused convulsions and death in some rabbits. The mosquitoes showed a marked dislike of feeding on treated animals, few did so and these took smaller blood meals than normal.

J R Busvine

GRANETT, P & SACKTOR, B **Testing Tick Repellents and Observations of Phototropic Effects** *J Econom Entom* 1947, Apr, v 40, No 2, 259-63, 9 figs

In experiments on the efficacy of chemicals as repellents of adults and nymphs of the tick *Amblyomma americanum*, it was observed that the animals were apt to move towards the greater light intensity, i.e., they exhibited positive phototaxis. [The authors' use of the word "phototropism" for this behaviour is to be deplored, as experimental workers restrict the term "tropism" to bending movements such as those exhibited by plants in response to light.] Unless illumination is controlled, phototactic responses may greatly confuse work on repellents.

Kenneth Mellanby

BRENNAN, J M **Preliminary Report on some Organic Materials as Tick Repellents and Toxic Agents** *Pub Health Rep Wash* 1947, Aug 8, v 62, No 32, 1162-5

Fifteen chemicals, including several found effective against other pests, were tested for repellency and toxicity to the ticks *Amblyomma americanum* (lone star tick) and *Dermacentor andersoni* (Rocky mountain wood tick). Most of the materials applied to socks, etc., gave 95 to 100 per cent protection for four weeks following treatment. Rinsing in warm tap water, however, removed most of the protective effect.

None of the compounds immobilized adult ticks confined on treated cloth within two hours, but several stopped nymphs in fifteen to thirty minutes.

The materials included dimethyl and dibutyl phthalates, phenyl cyclohexanol and benzyl benzoate. There were insufficient data to determine the most satisfactory repellent, but a mixture of phenyl cyclohexanol and butylacetanilide seemed most promising.

J R Busvine

HEWLETT P. S. & PARRIS R. A. The Formation of Insecticidal Films on Building Materials. II. Tests of the Efficiency of various Types of Pre-treatment. *Ann. Applied Biol.* 1947 May v 34 No. 2, 224-32, 1 fig

When the surfaces of building materials (brick, wood cement, etc.) are sprayed with insecticides to give a residual film, much of the liquid is absorbed into the more porous materials and the availability of the insecticide is lost. In a previous paper (PARRIS and HEWLETT *Ann. Applied Biol.* 1946, v 33 381) the authors showed that pre-treatment of the building surfaces allowed more effective and persistent films of DDT and pyrethrum to be applied.

In this paper further substances supplied by manufacturers were tested for pre-treatment effectiveness in improving film formation of pyrethrum in white oil P31. The flour beetle *Tribolium castaneum* was used as the biological indicator.

Thirty substances were subjected to preliminary tests and seven were examined more carefully. It was decided that the necessary qualities of the pre-treatment coating material were that it should be (1) relatively impermeable to the insecticide, and (2) wetted by the insecticide. The two most promising materials were 10 per cent. size and 5 per cent. gelatin—these will be examined further.

J. R. BARNES

## REPORTS SURVEYS AND MISCELLANEOUS PAPERS

SOUTHERN RHODESIA. Report on the Public Health for the Year 1946 [MORRIS, R. M. Medical Director & Chief Health Officer] 50 pp. 1947 Salisbury Rhodesian Printing & Publishing Co. Ltd.

*General*.—In April Dr. R. M. Morris took over the duties of Medical Director and Chief Health Officer from Dr. Martin who had held the position for 10 years. During 1946 the Commission under the chairmanship of Professor C. M. F. Saint, C.B.E., F.R.C.S., issued their report on the National Health, and another Commission, with Dr. A. J. Orenstein, C.B., C.M.G., C.B.E., as chairman reported on the Colony's leprosy services.

Two new medical stations have been opened: one at Antelope Mine for the Matobo Native District with a European community and over 80,000 Africans; the other at Karoi for the settlement there and for the Miami Mica fields and the African reserves of the Zambesi Valley.

*Vital Statistics*.—The figures for 1946 are inserted in brackets after those for 1945 for purposes of comparison. The European population at the end of June was 83,450 (80,330). Asiatics 2,940 (2,570). Coloured persons 4,580 (3,970). native Africans 1,687,000 (1,380,000). European births 2,147 (1,783). birth rate 25.7 (25.4). European deaths 687 (696). crude death rate 8.2 (10.0). infant mortality rate per 1,000 live births 30 (43) the lowest ever recorded in Southern Rhodesia. maternal deaths 4 (7). maternal mortality rate 1.9 (4.0). The chief causes of death among Europeans were heart disease and cancer, and of infants premature birth and congenital malformations. four of the 65 infant deaths were due to malaria.

*Diseases*.—There were no cases of smallpox among Europeans, but 181 among Africans, with only 1 death. *pulmonary tuberculosis* 36 cases, 3 deaths among Europeans, 323 cases, 89 deaths among the Africans showing how much greater is the fatality rate among the latter. Of the infective diseases of childhood, chickenpox heads the list with 824 cases, 247 Europeans and 577 Africans. Measles is next with 345 Europeans and 433 Africans. diphtheria 282 cases

(51 Europeans, all recovering, 231 Africans with 40 deaths) comes third, *whooping-cough* is fourth, but far behind the others, with 190 cases (84 and 106 respectively) and *typhoid fever* accounted for 108 (24 Europeans, 1 fatal 84 Africans, 9 fatal). There were 30 European and 16 African cases of *acute anterior poliomyelitis*, one death occurring in each group. *Scarlet fever* shows, as elsewhere in the tropics, the greater susceptibility of the European, there was only one African case to 62 European cases, but none was fatal. Admissions of Europeans for *malaria* numbered 1 116, the lowest for 5 years, and for *blackwater fever* 9, the lowest ever recorded in the Colony. It is hinted that this last may be due at least in part, to the scarcity of quinine and its replacement by mepacrine. *Leishmaniasis* is the chief vector of malaria. A Research Unit has concentrated on *schistosomiasis*, carrying out treatment of patients and destruction of snails in the same area. Sodium antimony tartrate (SAT) is used, in three injections given slowly on one day only, to a total of 1 grain for each 20 lb body weight, designed to destroy the female worm and so stop egg-production. Some physicians gave larger total doses of 1 grain per 12 lb body weight, but this seemed to entail greater risk. No case of *plague*, human or rodent, has been reported. Thirteen cases of *trypanosomiasis*, 5 fatal, have been notified, the highest for 35 years all from the Zambezi Valley areas. At the beginning of the year there were 1,004 *leprosy* cases registered at the three institutions, Ngomahuru, Myeniwa, and Mnene. Five of them were in Europeans. During the year 269 patients were admitted, 140 re-admitted, 84 discharged, 56 died and 51 deserted, leaving 1,222 on the register at the end of the year [not 1,223 as stated].

**Hospitals**—There are 14 Government hospitals, European admissions to them totalled 12 236 [elsewhere stated as 11 966], or 1.46 per mille, in 1941 the respective figures were 11,391 and 164. Maternity beds have been reduced to 118 by the closing of one private maternity home. Native hospital admissions totalled 36,311 and there is much overcrowding. Much medical aid is afforded by *native clinics*, of which there are 73 applications have constantly been made for more to be inaugurated. Inpatients at these numbered 71 620 and outpatients 245,138. Medical Mission clinics 37 in number, subsidized by the Government, provide 587 beds for Africans during the year, admissions to these totalled 29,657 and outpatients 166,399.

In the mules 70 545 were employed 1 284 fewer than in the preceding year, deaths 522 (564) were fewer and the rate 7.4 (7.85) per mille was lower. Venereal diseases are increasing both gonorrhoea and syphilis are common in the towns and the mining areas the main reservoir being native prostitutes. **Laboratories**—There are three routine laboratories all of which have done excellent work with a small staff assisted by Africans who have proved apt pupils at routine microscopical examinations. Details of the numbers of the different samples and specimens examined are given in lists in Appendices to the report.

**Schools**—There are three medical inspectors of schools and school children and a fourth is to be appointed when a suitable candidate can be found. There is a Government *Dental Service* with a staff of four qualified dentists whose time has been fully occupied in dealing with over 12,000 children and many other patients.

**Health Inspectors** do a vast amount of good work. Though there is only an establishment of 16, they inspect premises and supervise general sanitation, food and slaughter-houses. They perform vaccinations against smallpox (347,570 in the year) and against diphtheria (44,230). They have made 23,000 collections of mosquitoes. In some of these activities, they are assisted by Africans.

Nurses are overworked of a trained staff establishment of 145 only 128 are on the permanent staff nevertheless this is a great improvement on the previous year when there were only 65. To relieve the pressure, it has been found necessary to engage a number of midwives in the larger maternity homes although they have neither medical nor surgical qualifications. Training of nurses is carried on at Salisbury and Bulawayo hospitals of 50 candidates at the preliminary examination, 36 passed of 20 up for the final, all passed, 11 of them with honours. African males are also trained to become nursing orderlies, 31 presented themselves for the lower examination and all but two passed, as did 10 out of 11 at the higher examination.

H. Harold Scott

CONGO BELGE. Rapport sur l'Hygiène Publique au Congo Belge pendant l'année 1945. [Report on the Public Health in the Belgian Congo during 1945.] [LAMBRICHTS, G. P.] 140 mimeographed pp.

In a preliminary note Dr Lambrechts points out that it was possible to publish the 1945 and 1946 reports only in 1947 the 1945 report is concerned solely with statistics commentaries for both years together will be found in the 1948 report.

The 1945 report is a very complete statistical statement and contains a great deal of information in many cases covering several years. It is on similar lines to the statistical section of the combined report for the war years 1940-1944 [this Bulletin 1947 v 44 1024]

H. J. O'D. Burke-Gaffney

i. PATERSON A. R. The Human Situation in East Africa. Part I. On the Increase of the People. Part II. Towards a Population Policy East Africa Med. J. 1947 Feb & Apr v 24 Nos. 2 & 4 81-90 144 51

— Summary of some Figures and Opinions bearing on Population Growth. Ibid. 1947 Feb v 24 Nos. 2, 90-97

ii. BRITISH MED. J. 1947 Aug 9 14-15. Planning and World Population.

iii. MACDONALD G. Planning and World Population. [Correspondence.] Brit Med J. 1947 Sept. 27 506-7

i. These papers by former Director of Medical Services of Kenya form detailed consideration of the statements, quoted from the Governor of Kenya, that it is now evident that taken as a whole East Africa is barely able to support itself in food at the present time and that an ignorant man and his wife with a hoe are totally inadequate foundation for an enlightened state of society.

There is little doubt that the population of Kenya, and of East Africa as whole is now increasing at a rate which, if it persists, will present a continuously serious problem in relation to food, agriculture and soil productivity. The rate of increase has been estimated at between 1.5 and 2.3 per cent. per annum. These rates would raise the population of East Africa from just under 12,000,000 in 1935-6 to 34,000,000 or 50,000,000 respectively in 70 years. Public health measures and freedom from local internecine war will tend to remove certain checks on the growth of population, but the pressure of population unless it is accompanied by vigorous and enlightened agricultural policy will result in food shortage and its sequel, disease which would go far to neutralize public health effort.

Meanwhile according to the author the fertility of the soil of Kenya is declining by 50 per cent. we are told in the past twenty-five years. (The authority for this is not quoted, and to a reader the bald statements sometimes

made, that the soil of East Africa is naturally poor, are unsatisfactory in the absence of detailed information or proof.] The policy advocated by the author in the face of this most serious threat to the social and economic life of East Africa comprises a complete, synchronized and integrated policy of modernization such as was outlined by NOTESTEIN [this *Bulletin*, 1945, v 42, 507] Eventually, the size of families among the Africans will need to be curtailed, but to preach that doctrine to Africans now would be to invite the comment that the object of limitation must be to exterminate them. Control of size of families must therefore be induced by indirect means, by general education and general improvement in conditions of life.

Details of the programme of modernization are quoted from Notestein's paper, but are too full for reproduction here, they include proposals for industrial development and for social advancement.

ii In the editorial article, similar points are made, and the papers of Paterson are quoted along with others on India and elsewhere. Again are stressed, in relation to East Africa, the three factors: exhaustion of fertility of the soil because of the absence of fallow, ignorance of satisfactory methods of agriculture, and the high rate of increase of the population. The editorial ends as follows: "Yet unless the birth rate falls in relation to the death rate and the population problem is solved much talk about colonial development and welfare is, to use an American expression, 'whistling in the wind'."

iii Macdonald takes exception to the point of view displayed in the editorial article referred to. He admits that at present rates of increase of population there will come a time when population pressure is too much for the capacity of the land, but he argues that so much of East and South-East Africa is undeveloped, and that so much could be developed with comparative ease if simple methods of tapping ground water were adopted on a sufficient scale, that to speak of reducing population increase is at least premature. He points out that population densities in East Africa vary from 41 to the square mile in Uganda to 5 in Northern Rhodesia, and that enormous tracts of country are uninhabited. "The population problem is one of balance, and the economy of grossly undeveloped countries can be improved more readily and more to the general advantage of the world by an increase in the supportive capacity of the land than by a restriction of population, though ultimately that must come."

*Charles Wilcocks*

CAROTHERS, J. C. *Age and Wisdom Teeth in Africans* *East African Med J* 1947, Aug, v 24, No 8, 304-6, 1 graph

Medical practitioners in East Africa are frequently faced with the problem of giving an opinion on the age of Africans. This may be a serious responsibility, especially in adolescents, since the law for many purposes regards the East African as being adult if he is apparently 18 years of age or older. Many factors are required in framing an opinion, but there are often great difficulties. If it could be found that wisdom teeth erupted with some constancy at certain ages in Africans, they might prove a useful guide.

The author counted the wisdom teeth of 150 African boys admitted to a High School in Kenya. Many of them claimed to know the date of their births, although the author admits that this unsupported evidence detracts from the value of the enquiry, he has no reason to doubt that they were speaking the truth.

The boys represented a fair sample racially of the population of Kenya. They were mostly between the 15th and 22nd years of life.

The development of the wisdom teeth is shown in a table and depicted in graphic form. From the evidence available, the author observes that "one might draw the following very tentative conclusions —

- " 1. The African's wisdom teeth erupt with some constancy between the 15th and 21st birthdays.
- " 2. If an African has no wisdoms he is unlikely to be more than 20 years old.
3. If an African has all his wisdoms he is unlikely to be less than 17 years old.
- " 4. If an African has some of his wisdoms only he is unlikely to be more than 20 or less than 15 years old.

[This form of enquiry merits further investigation on a wide scale, in the search for a solution to a problem so familiar and often so perplexing to medical officers in Africa.]

H J O'D Burke-Gaffney

BOARD OF TRADE. German Industry. B.I.O.S. Final Report No. 1387 Tropical Medicine at Hamburg and Elberfeld. [Reported by F Hawking.] 28 mimeographed pp., 3 diagrams. 1947 London H.M. Stationery Office. [2s. 6d.]

WANYORI L. L. Contribución al estudio del problema de saneamiento en Venezuela. [The Health Problem in Venezuela.] XII Conferencia Sanitaria Panamericana. Cuadernos Amarillos. Publicaciones de la Comisión Organizadora. No 28 Caracas. 1946 70 pp. numerous charts, figs. & maps.

Venezuela is a country of 912,050 sq. kilometres and a population, in 1941 of 3,849,919. The density of population varies greatly but is well shown in sketch map with varying shading. During the quinquennium 1940-44 the chief causes of death were diarrhoea and enteritis [the former is rather a symptom than a disease] tuberculosis, heart disease, pneumonia and malaria. About 5 000 deaths occur annually from water-borne diseases—enteric fever or dysentery (amoebic and bacillary) and infantile diarrhoea.

The Ministry of Health and Social Assistance was created in March 1936 and a Division of Malariology the same year and of Sanitary Engineering in 1937. In 1942 a Division to deal with the hookworm question was set up. The need for the last will be clear when we are told that *Necator* infestation ranges between 17 and 91 per cent., with an average for the country of 52 per cent. that a census of houses revealed that of a total of 668,836 there were 509,308, or 76 per cent. without any arrangement for disposal of excreta. Details of faecal examination of over 13 000 specimens in 46 localities are given in a table, in 8 localities every specimen revealed a positive result and in 29 other localities there were 91-99 per cent. positive. A series of graphs shows the prevalence of this and other helminths in the different districts.

H Harold Scott

FAIRLEY N. H. Advances in the Treatment of Tropical Diseases. *Practitioner* 1947, Oct., v 159 No 95, 238-77 [39 refs.]

# TROPICAL DISEASES BULLETIN

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[No 2

## AVOIDABLE MENINGITIS

MEMORANDUM DRAWN UP BY THE PUBLIC HEALTH LABORATORY SERVICE AND  
THE LONDON SECTOR PATHOLOGISTS' COMMITTEE \*

Every operative procedure entails some risk to the patient, but in simple operations like spinal puncture the risk ought to be practically negligible. The occurrence of meningitis following the withdrawal of cerebrospinal fluid or the administration of a spinal anaesthetic is a grave reflection on the methods used in many hospitals, because these "accidents" can be avoided by the adoption of a simple and reliable technique. That such a technique is not in fact universally employed is attested by the number of cases of avoidable meningitis reported in the literature during the past few years. Furthermore, as Garrod (1946) points out, "There is a natural reluctance to publish anything which may appear discreditable. It is therefore probable that meningitis following spinal anaesthesia has been far commoner than the literature of the subject would suggest." This statement is endorsed by surgeons and anaesthetists whenever the subject comes up for discussion.

### *Nature and Sources of Infection*

This memorandum is not concerned with meningitis secondary to some primary infective focus already present in the patient at the time of operation. It refers solely to meningitis that results from the direct inoculation of micro-organisms into the spinal canal. The organisms most frequently incriminated are *Ps. pyocyanea* and related organisms which can multiply in water at room temperature, less frequently staphylococci and other skin contaminants may be responsible. Some of the water bacteria fail to grow in ordinary culture media incubated at 37°C, hence many cases have been diagnosed as irritative or aseptic meningitis which were probably the result of bacterial infection of the meninges. Organisms normally regarded as non-pathogenic may produce infection if they gain access to the very susceptible meninges.

The sources of contamination may be listed as follows —

- (1) Apparatus inefficiently sterilized or contaminated during use
- (2) "Sterile" water or saline used to rinse the apparatus
- (3) Hands of operator and assistants
- (4) Skin of patient
- (5) Anaesthetic, antibiotic or other solutions

[\* This memorandum supplements the recommendations of the Medical Research Council in their report (War Memorandum No 15) on "The Sterilization Use and Care of Syringes" (see this *Bulletin* 1945, v 42 843). Certain minor changes in the wording of two sentences have been made with permission, in view of the special interests of readers of this *Bulletin*. Ed.]

### Precaution Measures

The ideal would be to adopt the full aseptic ritual of a surgical operation for every spinal puncture. In many cases the time and place render this impossible. The following recommendations are therefore offered, not necessarily as ideal procedures but as practical methods applicable in nearly all circumstances.

(1) *Apparatus*.—If facilities are available, all apparatus including manometer should be enclosed within suitable containers and sterilized either by autoclaving at 15 to 20 lb. pressure for 20 minutes or by dry heat at 160°C. for an hour. The complete outfit can then be held ready for use at any time. If dry heat is used, the rubber tubing of the manometer should be sterilized by boiling. For syringes and needles dry heat is preferable but ordinarily necessitates the use of all-glass syringes. (Glass syringes with metal nozzles, which will withstand dry heat at 160°C. for 2 hours are now being manufactured.) Full details of these methods, together with recommendations for a hospital syringe service, are given in the Medical Research Council's War Memorandum No. 15 (1945) on "The Sterilization, Use and Care of Syringes".

If autoclaving or dry heat sterilization cannot be employed, all apparatus should be sterilized immediately before the operation by boiling for 5 minutes, preferably in distilled water. A sterilizer with a perforated lift-up tray should be used. At the end of boiling the tray is removed, placed in the inverted lid, covered with a sterile towel and left to cool.

In the occasional emergency which may arise in the patient's home a perfectly clean saucepan with a lid may be used. After boiling, the water should be drained off and the saucepan left with the lid on until cool. Methods of chemical disinfection such as soaking in spirit should not be used.

(2) *Sterile Water and Saline*.—These probably constitute the greatest source of danger. Hospital supplies are frequently contaminated either from inadequate sterilization initially or from contamination during previous use (SMITH and SMITH, 1941). Thus the Winchester bottle of sterile distilled water or saline, used repeatedly until empty, has frequently been incriminated as the source of water bacteria found in contaminated or infected cerebrospinal fluid. If apparatus is sterilized as recommended above rinsing and cooling solutions become quite unnecessary and their use should be abandoned.

(3) *Hands of Operator*.—The operator should scrub up as for a major operation, or alternatively should don dry sterile surgical gloves. When gloves are not available it is important that his hands be dry before he handles any apparatus: this may be accomplished by rinsing with industrial spirit and/or drying with a sterile towel. Where needle and syringe have to be assembled, the needle should be handled with sterile forceps. From this point onwards the operator should touch nothing except the sterile instruments and the skin of the patient until the operation is finished. The trocar when withdrawn should be laid on a sterile towel: otherwise it may infect the spinal fluid if it is introduced again to clear the needle.

(4) *Skin of Patient*.—Thorough washing with soap and warm water followed by thorough, not perfunctory, swabbing with tincture of iodine or 70–80 per cent. alcohol will leave little risk of contamination of the needle by the patient's skin. The area treated should be the entire area exposed and the skin should be quite dry before puncture is made.

(5) *Anaesthetic and Antibiotic Solutions*.—No cases of meningitis have been traced to the presence of bacteria in anaesthetic solutions contained in sealed glass ampoules. Such ampoules are preferable to rubber-capped bottles intended for repeated use.

The sterilization of the outer surface of an ampoule is difficult and attended with such pitfalls that it is better not to attempt it. The ampoule should be



opened, after swabbing the neck with 70 per cent alcohol applied with sterile swabs, by an assistant whose hands have been scrubbed and dried. It may be held in a sterile towel or piece of sterile lint. The operator must then introduce the needle of the syringe into the ampoule without fouling the mouth.

Other forms of container should be avoided except where absolutely necessary. If a rubber-capped bottle has to be used, it should be held in a sterile towel by the assistant, and the cap should be thoroughly swabbed with 70 per cent alcohol or tincture of iodine. It is unwise to use rubber-capped bottles for more than a short time, and they should be replaced frequently, or, if the contents permit, returned to the central sterilizing depot each day for complete sterilization by an appropriate method.

The intrathecal injection of antibiotics such as penicillin and streptomycin demands the same high standard of aseptic technique, and all precautions should be taken to ensure that the solutions themselves are sterile.

### *Reporting of Cases*

The general adoption of the measures recommended here would, without doubt, reduce the incidence of "accidental" meningitis but would not close every possible loophole for infection. Further safeguards can be found only if cases are thoroughly investigated as and when they occur and with the employment of specialized bacteriological methods. The Public Health Laboratory Service will willingly co-operate with the hospital pathologist or other officer in carrying out such investigations as are required.

Gratitude is expressed to Sir Hugh Cairns and Professor Wilson Smith for the help they gave in the preparation of this memorandum.

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## SUMMARY OF RECENT ABSTRACTS\*

### II YELLOW FEVER

#### *General*

CECCALDI (p 75) reports that a small experiment suggested that penicillin may have some slight virucidal action on the yellow fever virus.

PERLOWAGORA and HUGHES (p 657) discuss a complement-fixation test for yellow fever, in which they have used the globulin fraction of a mouse-brain antigen. This test becomes positive after even mild attacks of yellow fever, but rarely after vaccination with 17D. It should prove useful in epidemiological studies, for tracing comparatively recent cases of yellow fever.

#### *Epidemiology Epizootology Transmission*

MAHAFFY *et al* (p 72) have brought together the results of mouse-protection tests performed on sera from various parts of East Africa, which have helped to define the areas in which yellow fever has occurred recently. These areas extend from the Belgian Congo to the Sudan and Eritrea, as far south as Northern Rhodesia, over a far wider area than would be suspected on the

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\*The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin* 1947 v 44. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

evidence of clinical diagnosis. The authors point out the important fact that a high proportion of cases in Africans are mild, and that mild yellow fever cannot be diagnosed clinically.

HADDOW *et al.* (p. 992) state that continuous studies made in Uganda have shown that, of the many groups of animals investigated, yellow fever immunity is found only in monkeys. The important species in this respect are *Cercopithecus mitis* *impungus* and *Colobus polykomos* *salicinus*. The species of mosquitoes chiefly suspected of transmission from monkey to monkey are mainly arboreal, and investigations indicate that *Aedes africanus* may be the principal vector in this animal community. It seems likely that the *Colobus* monkeys are the chief species involved in the monkey-to-monkey cycle in uninhabited forest areas, but that the *Cercopithecus* monkeys are important in bringing the virus into contact with man. SMITHBURN and HADDOW (p. 71) have found yellow fever virus in wild-caught *Aedes simpsoni* and in *Aedes* of other species (excluding *egypti*) in Western Uganda. They give reasons for thinking that *Aedes africanus* may be implicated. There is apparently an extra-human cycle of yellow fever in monkeys and mosquitoes in the Semliki forest. HADDOW *et al.* (p. 516) have investigated the vertical distribution and the biting cycle of mosquitoes in an area of rain-forest in Uganda. Catches were made up to 80 feet from the ground, and the mosquitoes caught were identified, pooled, and injected into monkeys to test for yellow fever virus. This was found in only one batch of *Aedes* species, containing, among others, *Aedes africanus* a known potential vector. *Aedes africanus* is the commonest arboreal culicid, and is most abundant 50-80 feet from the ground. In the area studied the monkey population is about 400 to the square mile. The authors give much information on temperature and humidity and on the biting-times of the various mosquitoes. They note that *Anopheles gambiae* is by far the commonest mosquito even far from human haunts.

BAILEY (p. 657) reports a study of the *syrian* mosquitoes of Gede, a settlement in forest country on the coast of Kenya. *Aedes* species haunt the upper forest strata.

LEWIS (p. 656) gives much general information on mosquitoes of the Sudan in relation to yellow fever and includes a list of the known vectors but the paper cannot satisfactorily be abstracted further. Mosquito control in the Sudan has rendered impossible an urban epidemic transmitted by *Aedes aegypti* and has eliminated this mosquito from the river steamers.

DURIKUX *et al.* (p. 991) found protective antibodies in 88 per cent. of a series of baboons (and one other monkey) in French territory near the Gambia. They note that the percentage usually recorded is of the order of 20-25 per cent., and they make the point that further investigation indicated that the positive results could not be explained by the presence of non-specific substances in the sera. Wild animals are evidently important as reservoirs in this part of Africa.

TAYLOR *et al.* (p. 414) undertook an extensive investigation in the State of Bahia, Brazil, in which they found evidence of jungle yellow fever spreading to man in the absence of *Aedes aegypti*. Positive neutralization tests were found in man, most commonly in adult males who frequently visited those forests which are more than 75 years old. Many mammals and mosquitoes were collected and tested, but although protective bodies (which were probably not specific) were found in certain rodents, the only definite evidence of transmission was in relation to marmosets (of which four *Callithrix penicillata* were found with circulating virus) and *Haemagogus papuanus* (from which virus was obtained). There is, therefore, a close relationship between immunity in man and marmosets, the prevalence of *Haemagogus* species, and the older climax type of tropical rain-forest. WADDELL and TAYLOR (p. 309) think that the marmosets *Leontocercus chrysomelas* and *Callithrix penicillata* are the principal,

if not the sole, vertebrate hosts of the yellow fever virus in part of the State of Bahia, Brazil

BATES and ROCA-GARCIA (p 310) think that the opossums *Metachirus* and *Caluromys* are the two most susceptible Colombian marsupials, but even with these, infection of *Haemagogus* mosquitoes is difficult, so that it is doubtful if the local marsupials are important in the *Haemagogus* cycles in nature. On the other hand, the cycle was easy to maintain with certain monkeys and marmosets. [but see below] ANDERSON and ROCA-GARCIA (p 992) show that the opossum *Caluromys langger* is susceptible to infection with yellow fever virus, although the infection is not fatal. After injection of virus, in most cases the virus circulates in the blood for several days, and specific neutralizing antibodies appear later. Some of the animals maintain the neutralizing antibodies, but in others the antibodies decrease and may disappear, in which case the animal may once more become susceptible to infection. Certain anomalies were found in a proportion of the animals, in relation to infection and immunity, but the majority reacted as described.

ANDERSON and OSORNO-MESA (p 309) note that other workers have shown that *Haemagogus spegazzini falco* and *H. equinus* are capable of transmitting yellow fever virus, and report that they themselves have proved *H. splendens* also to be capable of transmitting the virus under laboratory conditions. BATES and ROCA-GARCIA (p 308) have noted that *Haemagogus* mosquitoes fed on Saimiri monkeys infected with a pantropic strain of yellow fever virus rarely become infected themselves, and in a series of experiments with French neurotropic virus passaged in Saimiri monkeys, they failed to demonstrate infection in any of the *Haemagogus* mosquitoes subsequently fed on them.

In a study of the infection of *Haemagogus* mosquitoes with yellow fever virus, the same authors (p 415) have shown that the virus diminishes in amount in the mosquitoes for a few days after ingestion, and may even die out altogether, but that multiplication then takes place very slowly, and the mosquito may become infective by bite 10-28 days after infection. These processes depend very largely on the environmental temperature, and the temperature range found in nature in the haunts of *Haemagogus* species not only favours the development of the mosquitoes, but also of the virus in them.

SNIJERS *et al* (p 993) report on protection tests carried out in Surinam, where they indicate the presence of jungle yellow fever.

KOPROWSKI (p 580) comments on the fact that the sera of various animals have shown virucidal properties against the yellow fever virus, even though the animals have never been infected. He shows that many of these sera are virucidal also to certain other viruses which are not found in the countries concerned. This non-specific virucidal property is transitory, and the animals concerned react specifically to injection of yellow fever virus.

#### Vaccination

FOX (p 1062) has studied the factors which influence the multiplication of virus 17D in tissue cultures, but details of his findings must be sought in the original. FOX and LAEMMERT (p 1062) report observations on the infection of developing chick embryos, but these again must be sought in the original. They make the point that prolonged embryo-to-embryo passage of strain 17D, and the French neurotropic strains, did not reveal significant changes in the character of the virus. It is still unknown by what means the attenuated variants of yellow fever virus (such as 17D) may be produced, continuous embryo passage usually fails to produce them.

BURRUS and HARGETT (p 994) have found that 17D vaccine virus may be desiccated at room temperature without more loss than occurs at lower temperatures, but they advise that it should then be stored at  $-20^{\circ}\text{C}$  to  $-25^{\circ}\text{C}$ .

Adequately desiccated vaccines may remain potent enough for use even if kept at tropical temperatures for a few weeks, but great loss of virus does take place under these conditions. When the vaccine is diluted for use, 1:1 or 1:10 dilutions should be used within one hour and 1:100 within 10 minutes.

PALTIER (p. 417) describes the preparation of the dry mouse-brain vaccine made in Dakar. The brains of mice which have been inoculated intracerebrally and which show paralysis, are desiccated, ground with an inert powder and kept at  $-4^{\circ}\text{C}$ . to be reconstituted, for scarification, with a gum solution. This vaccine is sometimes mixed with smallpox vaccine. LAURET (p. 580) does not approve of the mixing of smallpox and yellow fever vaccines, for scarification, because he believes that the neurotropic properties of each may thus be enhanced.

In the *Epidemiological Information Bulletin* (UNRRA Health Division) (p. 73) there is a detailed account of a series of comparative tests of the neurotropic brain vaccine made at Dakar and administered by scarification, in a gum solution with or without smallpox vaccine and of the American 17D vaccine given subcutaneously. The Dakar vaccine was undoubtedly a potent immunizing agent, producing neutralizing antibodies in the serum of practically 100 per cent. of the subjects tested. But vaccine 17D also produced neutralizing antibodies in practically 100 per cent., and it has shown itself to be a powerful immunizing agent in the field. 17D does not produce encephalitis, which has been reported after the use of mouse-passage neurotropic vaccine mixed without immune serum. Each of these vaccines is unstable at temperatures above  $5^{\circ}\text{C}$ . but can be kept for long periods if dried and frozen. In a long comment on this paper MACCALLUM discusses the history of yellow fever vaccination. The intraperitoneal mouse-protection test appears to be more sensitive than the intracerebral test, in detecting neutralizing antibodies.

ANDERSON and GAST-GALVIS (p. 613) have investigated the state of immunity of people vaccinated about 5 years previously in Colombia. They found evidence of neutralizing antibodies in some 83 per cent., and show that there is no essential difference in response between children and adults. They conclude that revaccination is not usually necessary within 5 years of vaccination with 17D.

#### Control

FINDLAY (p. 579) discusses the spread of yellow fever and other diseases by aircraft and suggests that an international organization should be formed under the W.H.O. to control airfields, disinsection of aircraft, yellow fever vaccine and vaccination certificates.

DE CALLES (p. 638) reports on the yellow fever service of British Guiana. He considers that DDT is one of the very important means of controlling *Aedes aegypti* but that much investigation remains to be done, for instance in relation to the ability of eggs of this mosquito to remain viable for long periods in dry conditions. In a later report (p. 664) he states that this service has now ceased to exist as a separate organization, having become part of the mosquito control service. The value of DDT is again emphasized, but control depends chiefly on a high standard of efficiency in all branches of the service, which has been attained. No case of yellow fever was reported in the Colony during 1948.

Charles H. Stocks

## MALARIA

BLACKIE, W K Malaria, with special reference to the African Forms

This book is reviewed on p 216

ASCOLI, Maurizio Nuove vedute sulla malaria Studi di Medicina e Biologia  
[New Outlook on Malaria] 211 pp, 24 illustrations 1946 Rome  
Istituto Bibliografico Italiana. [L 350]

This volume contains papers contributed to a Conference on Malaria convened in Palermo The first part (119 pages) deals with the rationale, application and results of the adrena-line treatment of malaria, with which the name of Ascoli is so closely associated There are 12 papers written by Professor Ascoli and ten of his collaborators, dealing with all aspects of the question Account is taken of the extensive literature concerning this method of treatment that has appeared during the last fifteen years, 191 references are listed This very complete exposition of the subject is deductive

The second part of the volume contains a paper by G BUONOMINI outlining modern conceptions of the cycles of development of malaria parasites in vertebrate hosts The same author with M MARIANI contributes a paper on the races of *Anopheles maculipennis* and anophelism without malaria in Europe G D'ALESSANDRO and M GRACOLICI deal with the suppressive use of anti-malarial drugs M ASCOLI and S SORCE describe an ingenious method of concentrating malaria parasites in Blood examinations by centrifuging citrated blood  
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ZOTTA, G, RADACOVICI, E, TEODORESCU, A M, GEORGESCU, M, MARDARE, I, DUPORT, M, ATANASIU, M & TRIFON, A Evoluția endemiei palustre în județul Teleorman [The Course of a Malaria Epidemic in Teleorman] Rev Stinfelor Med Bucharest 1946, Sept-Dec, v 36, Nos 9/12, 781-815, 9 graphs & 1 map French summary

Teleorman is on the left bank of the Danube between 1935 and 1942, there was an epidemic of malaria, in two phases, the first (1935-1938) was of moderate intensity and constant extent, the second (1939-1942) was more severe

In general, cases were seen mostly in river valleys and particularly those of the rivers Urlui, Calmatzuu and Teleorman, in the lower parts of which the flood areas of the Danube may also be included

The serious nature of the epidemic during the war years may be attributed, not only to war conditions, but to natural factors and also to man-made causes, particularly that of rice cultivation which was a recent introduction All along the rivers, the local inhabitants had constructed dams, which resulted in the formation of breeding places for mosquitoes

All human species of *Plasmodium* were found, except *P ovale*, the proportions varied each year In general, *P vivax* infections were commoner than those caused by *P falciparum*, except in 1936 (*P vivax* 624, *P falciparum* 772) and 1939, when the numbers were about equal (1,373 and 1,334) Quartan was rarely seen, and in 1939 was not reported at all

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and *A. m. maculipennis*. The first-named occurs in the southern flood-region where stagnant water is in evidence. Its rôle as a malaria vector is important, though not striking.

*A. m. atroparvus* is found throughout the Department wherever the soil is salty and the water covering it becomes brackish. It plays a predominant part in transmission throughout the year.

*A. m. maculipennis* is predominant in the northern half of the Department. While it is not in general regarded as a vector, it must be suspected to play an important rôle among a population who are so much exposed to it outdoors where they sleep in the summer without providing themselves with any protection against it.

H. J. O'D. Burke-Gaffney

SIRRE G. & TWINKING. May. Survey and Field Treatment of Malaria in Mauritius. pp. v+78, 50 figs. & 5 pls. 1948. Published on behalf of the Government of Mauritius by the Crown Agents for the Colonies. London 4 Millbank, S.W.1 (25/- or Rs. 16.67)

This is the most comprehensive survey of malaria in Mauritius yet published. The survey was undertaken at the request of the Military Authorities when it became necessary in 1942, to post troops and labour gangs in certain of the coastal areas where malaria was rife. The detailed work of the survey was carried out by three V.A.D. assistants and three male laboratory assistants. In assessing the incidence of the disease children from two to ten years of age were examined. To study the development of immunity babies from birth to two years of age and persons from eleven to twenty years of age were examined.

Mauritius is an island of volcanic origin, 700 square miles in extent with a high central plateau. In the north and south-east there are large areas below the 600-feet level elsewhere the coastal plain is narrow. At high altitudes the annual rainfall exceeds 150 inches. There are numerous small rivers and streams, and irrigation canals for sugar cane. In the coastal belt the drainage is poor. The population is about 400 000 (600 to the square mile) 70 per cent. of whom are Indians.

Malaria-carrying mosquitoes were introduced into Mauritius in 1865 either from Madagascar or from East Africa. The result was devastating. In 1866 the death-rate for the whole island was 32.1 per thousand. In 1867 it rose to 120.5 per thousand. It was, however, not until 1869 that the disease completely encircled the island. Since then malaria has been very largely confined to the coastal belt. It was so when Ronald Ross made his survey in 1908. Small outbreaks of great intensity have occurred, however, from time to time at higher altitudes. Thus at Alma, 1,500 feet, a severe outbreak occurred during the first quarter of 1943 when a thousand cases were notified in a camp with a strength of 1,200. The spleen rate was 90 per cent.

The two malaria vectors are *A. gambiae* and *A. funestus*. *A. maculipennis* is only occasionally found. *A. mauritiana* [*A. constanti*] has not been shown to be a vector.

The average spleen rate of children living below 600 feet was 48 per cent. from 600 to 1,200 feet, 13. from 1,200 to 1,800 feet 8 (excluding Alma, on the occasion mentioned above) above 1,800 feet 7. Fifty nine per cent. of the population live below 600 feet, this area constituting a little more than half the total area of the island.

Below 600 feet the average parasite index was 36 per cent. (*P. falciparum* 48, *P. vivax* 35, *P. malariae* 32, mixed infections 14 per cent.). Above 600 feet, the parasite index was 12 per cent. (*P. falciparum* 40, *P. vivax* 43, *P. malariae* 21, mixed infections 16 per cent.)



Temperature appears to be the limiting factor in malaria transmission, there is but little transmission even at sea level in the winter. The breeding of *A. gambiae* may, however, occur as high as 1,500 feet when conditions are particularly suitable. The malaria "season" extends from December or January to the beginning of June.

A large proportion of the Mauritius population have a very poor nutritional standard, this probably accounts in part for failure to develop immunity. The maximum spleen rate in hyperendemic areas is reached at the age of five, very little reduction in spleen rate and no reduction in spleen size is seen even up to the age of 20. The parasite rate shows a very rapid rise to the age of four, thereafter there is a gradual decline. By the age of 14 it has fallen to half. The gametocyte rate curve corresponds with the parasite rate curve. Children between one and eight are the main danger to the community.

An interesting part of the report deals with the relationship between malaria and malnutrition. In villages with spleen rates below 20 per cent, nutrition was unsatisfactory in 2.4 per cent of children and borderline in 11.9 per cent. In villages with spleen rates above 20 per cent, nutrition was unsatisfactory in 6.8 per cent of children and borderline in 20.3. The commonest signs of malnutrition were mosaic skin, angular stomatitis and glossitis, and anaemia of the macrocytic type. Thirty per cent of children with enlarged spleens showed macrocytosis.

In the Black River District, where nearly all villages have spleen rates of 90 per cent or over, the infant mortality rate was 303 per 1,000 live births. In the Plaines Wilhems District, parts of which are almost malaria-free, the infant mortality rate was 114 per thousand.

As an emergency measure, children living in proximity to military areas were treated by a combination of drug therapy or extra feeding or both. When transmission was not excessive and nutrition was satisfactory, adequate control was secured with either quinine or atabrin [mepacrine]. Supplementary feeding with milk markedly increased the efficacy of drug treatment. Shark liver oil and yeast were also of value. Vegetable soup and yeast alone were both ineffective.

Norman White

SAUNDERS, G. M. & SCOTT, V. *Preservation of Plasmodium vivax by Freezing*  
*Science* 1947, Sept 26, 300-301

Protozoa, unlike viruses, are difficult to preserve for long periods in an unchanged condition. Low temperature freezing, however, has been successfully employed up to 70 days in the case of animal plasmodia. The authors use such a method for the preservation of *Plasmodium vivax*. The infected blood is taken into 4 per cent sodium citrate solution, in the proportion of 20 parts blood to 3 parts citrate. About 2-3 cc. of the citrated blood are put into small, plastic, screw-capped vials and the blood is rapidly frozen at a temperature of  $-75^{\circ}\text{C}$  by immersion in a mixture of alcohol and dry ice, then stored in a dry-ice box at  $-50^{\circ}\text{C}$ . Before use, the blood is thawed in a water-bath at a temperature of  $40^{\circ}$ - $42^{\circ}\text{C}$ . In this way, parasites remain viable up to 15 days or more and, in one case, up to 37 days.

The results indicate some modification from the normal in the ensuing infection, including, in at least one of 3 cases, a mild chill after inoculation. However, changes are only to be expected when it is considered that freezing and thawing cause almost complete haemolysis of the red blood cells and considerable modification in the staining reactions and morphology of the parasites.

P. C. C. Garnham

MOANA, E. Un nuovo metodo di produzione in vitro del processo di flagellazione dei microgametociti dei parassiti malarigeni. [Flagellation of Microgametocytes of Malaria Parasites *in vitro*.] *Riv di Parassit.* Rome. 1947 Mar v 8, No. 1 63-5.

Two or three drops of blood are removed from the comb or from a vein of the wing of a fowl infected with *Plasmodium gallinaceum* on to a slide and mixed with an equal quantity of a 3 per cent. solution of citrate of sodium. By rocking the slide, a homogeneous mixture is obtained. A very thin cover glass is placed on the mixture in such a manner that no pressure is applied. On examining the preparation microscopically it will be noted that the red cells arrange themselves in a floral design the centre of which will be found to be a flagellating microgametocyte. The observations were repeated with human blood containing *P. vivax* but the floral arrangement was not so marked as in the case of fowl's blood. As a modification of the method, the blood can be taken into a syringe containing the citrate solution and the mixture run on to the slide for observation.

C M Wesson

PAL, R. Marking Mosquitoes with Fluorescent Compounds and Watching them by Ultra-Violet Light. [Correspondence.] *Nature* 1947 Aug 30 298-9.

The author has shown that mosquitoes (*Anopheles maculipennis* var *atroparvus*, *Culex molestus* and *Aedes aegypti*) are not adversely affected by ultra-violet light, that they can take up enough fluorescent dust (anthracene and other substances) on their bodies to enable them to be observed at a distance of 10 feet in ultra-violet light, and that they are not adversely affected by the dust. Observations are therefore possible on the behaviour of mosquitoes at night which could not otherwise be made.

Charles W. Weeks

CHELĂRESCU M & CURPAN C. Varietățile de *A. maculipennis* din regiunea silvii, județul Sibiu. (Lucrare făcută sub conducerea Prof. M. CIUCA și Prof. L. BALLIU) [Types of *Anopheles maculipennis* in the Sibiu Region (Rumania).] *Rev Științelor Med.* Bucharest. 1947 Jan.-Apr v 36, No. 1/4 63-75. French summary (8 lines)

Studies made in August 1944 in a malaria-free area of the Sibiu region showed the following prevalence of anophelines: *Anopheles maculipennis maculipennis* 63.3 per cent. *A. m. messeae* 31.9 per cent. *A. m. atroparvus* 2.7 per cent. Examination of eggs also demonstrated the occasional presence of eggs having a different external configuration.

The first two species, when infected experimentally proved to be more resistant than homologous species from a hilly area (Socola-Lag).

H J O'D Burke-Gaffney

UNGUREANU E & SHUTE, P G. The Value of the Wing Scales as an Aid to the Taxonomy of Adult *Anopheles maculipennis*. *Proc Roy. Entom. Soc. London* Ser. B. 1947 Aug 15 v 16, Pts. 7-8, 79-85 1 pl. [10 refs.]

A paper by Ungureanu (1944) on the wing scales of the *Anopheles maculipennis* complex has already been noticed (this Bulletin 1947 v 44 857). The material on which the present studies were based was obtained from Rumania, England, Algeria, Holland and Italy—the collection from Albania in the London School of Hygiene and Tropical Medicine was also examined.

From the accumulated data on shape and size of wing scales, the authors have been able to construct a key which they claim is 90 per cent. accurate, for the identification of *A. maculipennis atroparvus messeae maculipennis* and

*clutus* (*sacharovi*) It is not yet possible to distinguish the larvae of these races except *clutus*, but keys are given for the separation of the eggs of the above and *labranchiae*, and for the identification of the males, the latter being based on details of the hypopygia

In view of the biological and morphological facts now known, the authors consider that the *A. maculipennis* group consists of at least four species rather than of varieties, *A. labranchiae* is not included yet, because sufficient material has not been studied and it can only be separated from *atroparvus* on egg characters. The wing scales of *A. m. maculipennis*, *atroparvus* and *messae* are shown in a photograph

H S Leeson

MATTINGLY, P F Notes on the Early Stages of certain Ethiopian Mosquitoes, with some Locality Records from British West Africa *Ann Trop Med & Parasit* 1947, Sept, v 41, No 2, 239-52, 4 figs [20 refs]

This paper contains a description of the larva and pupa of *Anopheles domicolus* and some corrections and additions to existing descriptions of the pupae of *A. wilsoni*, *A. nubi*, *A. hargreavesi*, *A. argenteolobatus* and *A. multicolor*. Some points of difference between the larvae and pupae of *A. turkhusi* and *A. luspaniola* are given and there is a note on the unreliability of the various criteria for distinguishing the larvae of *Aedes grahami* from other members of the subgenus *Mucidus*

The locality records include anophelines and culicines collected in British West Africa between September 1942 and December 1944, but do not include new records of anophelines already published by the author in 1944 [this *Bulletin* 1945 v 42, 434]. The present new distribution records are indicated in the concluding notes on species

H S Leeson

GELFAND H M Natural Malaria Infection in *Anopheles rufipes* (Gough) *J Trop Med & Hyg* 1947, Aug, v 50 No 8, 159-60

The author has found the type form of *Anopheles rufipes* infected at Kano, N Nigeria, and states that previous dissections of small numbers had always been negative. Larvae were found only in large, sunlit, stagnant pools with clean water and upright, grassy vegetation, often along with *A. funestus* but never with *A. gambiae*

*A. rufipes* may be found in human habitations at the end of the rainy season in N Nigeria, but in relatively small numbers only. *A. funestus* especially, and *A. gambiae*, are much more numerous. Its importance as a vector of malaria is probably slight

Charles Wilcocks

RAO, V V On Gonotrophic Discordance among certain Indian *Anopheles*. *Indian J Malariology* 1947, Mar, v 1, No 1, 43-50 [11 refs]

The author describes some preliminary work on *Anopheles annularis* and *A. culicifacies* to show that while in the autumn there is a certain amount of gonotrophic dissociation, there is no general suspension of sexual activity in any species *en masse*, but that some individuals among the Indian anophelines enter into a condition midway between gonotrophic dissociation and gonotrophic concordance. In a mosquito in this state, which he calls gonotrophic discordance, the development of the ovaries does not keep pace with the nutrition but is dependent on repeated feeding. Full ovarian development may only be completed after a prolonged period, and during this time the female feels no urge to leave its feeding place to lay eggs. The author therefore puts forward the hypothesis that, as repeated feeding would appear to increase the chances of

infection, it is the mosquitoes with suspended or delayed sexual activity which may alone be responsible for malaria transmission while the majority which remain sexually active, do not as a rule transmit the disease, but help to keep up the population.

The author is unable to pursue the matter further but hopes it will be investigated by other workers.

H S Lester

WHITE R. Senior. On the Anthropophilic Indexes of some *Anopheles* found in East Central India. *Indian J. Malariology* 1947 Mar v 1 No. 1 111-22. [21 refs.]

The results are tabulated of some thousands of precipitin tests on the stomach contents of sixteen species of *Anopheles* captured in East Central India. In the case of five of these species (*Anopheles culicifacies*, *fluviatilis*, *versus*, *minimus*, and *aureolaris*) the results of dissections are also given in order that the infection rate may be compared with the anthropophilic index. The figures are presented under three heads—houses, cattle-sheds and out-of-doors. The author suggests that the differences observed in tropisms and in vectorial capacity point to the existence of biological races among these species, though only in the case of *A. versus* has any evidence been recorded (egg measurements) which might support this view—these measurements are awaiting statistical analysis.

The information regarding the remaining eleven species is much less complete and no infection rates are given for comparison.

H S Lester

FERNÁNDEZ MELÉNDEZ, A. Aportación al estudio del *Anopheles vestipennis* en Cuba. [A Study of *Anopheles vestipennis* in Cuba.] *Typhlocyba sobre Malaria*. Venezuela. 1946 Sept. v 10 No. 3, 133-6.

In Cuba, *A. vestipennis* may be regarded as a much more important vector of malaria than was hitherto locally believed.

It shows a marked preference for feeding on human blood. *A. albimanus* shows no preference between human and animal blood, while *A. crucians* and *A. grahami* possess definite zoophilic characteristics.

Dissections of the stomachs and salivary glands of *A. vestipennis* gave negative results, indicating that malaria transmission by the species was not active during the course of these investigations.

H J O'D Burke-Gaffney

GABALDON A. & COYA-GARCIA, P. Zoogeografía de los anofelinos en Venezuela: III. Relaciones con el terreno y clima. [Distribution of Anophelinae in Venezuela: III. Meteorological Considerations.] *Typhlocyba sobre Malaria*. Venezuela. 1946, Sept. v 10, No. 3, 164-78.

BOTD M. F. A Review of Studies on Immunity to Vivax Malaria. *J. National Malaria Soc.* 1947 Mar v 6, No. 1 12-31 13 figs. [10 refs.]

In this address, the author brings together the important observations made by him and his co-workers on immunity to *P. vivax* infections during a prolonged experience of malaria therapy. A clinical attack of three weeks or longer after inoculation with *P. vivax* indicates that the patient was previously completely susceptible. Short attacks from one day to two weeks may follow either heterologous or homologous reinoculation, indicating in the latter case, that immunity is incomplete. Homologous reinoculation may be followed by no clinical attack or fail altogether—the latter indicates a very effective refractory condition. A comparison of the parasit density at the beginning and the end of the clinical attack shows that a tolerance to the presence of the

parasites is the first manifestation of developing immunity. Soon after the infection becomes latent, the host is able to destroy numbers of parasites enormously greater than the few which can initiate an infection in a susceptible person. This destructive mechanism does not seem to be operative against sporozoites, but the resulting trophozoites will quickly disappear. The state of complete refractoriness may be of considerable duration, there is no evidence that its persistence is dependent upon the persistence of latent infection. The failure of serum of hyperimmune persons to confer passive immunity on susceptible persons indicates that the immunity is not humoral.

The possibility of conferring active immunity by inoculation with killed parasites is difficult to determine. Two susceptible patients saturated with quinacrine, were each given three inoculations of living parasites, which were presumably killed *in vivo*. Subsequent reinoculation by infected mosquitoes was followed by only a short clinical attack in each case. *Norman White*

WHORTON, C M, KIRSCHBAUM, W R, PULLMAN, T N, JONES, R, Jr, CRAIGE, B, Jr, ALVING, A S, EICHELBERGER, Lillian & COULSTON, F  
**The Chesson Strain of *Plasmodium vivax* Malaria. I. Factors influencing the Incubation Period** *J Infect Dis* 1947, May-June, v 80, No 3, 223-7  
 [15 refs]

The Chesson strain of *P vivax* is of New Guinea origin. The observations recorded concerned psychotic patients in a hospital, and volunteer inmates of a penitentiary. Of 121 individuals receiving trophozoite infections, heparinized whole blood, 66 were inoculated with compatible blood, 55 with incompatible blood. The mean incubation period of the former group was 2.1 days, of the latter group 4.8 days. "Inoculation fever" is in most instances related to blood incompatibility. The incubation period varied inversely with the number of parasites in the inoculum.

In mosquito-induced infections there was a negative correlation between the approximate number of sporozoites injected and the length of the prepatent period. Three subjects who were bitten by from 45 to 80 heavily infected mosquitoes had prepatent periods of 9, 11 and 12 days as compared with the mean prepatent period of 13.6 days in 139 individuals each of whom was infected by the bites of 10 infected mosquitoes. *Norman White*

CRAIGE, B, Jr, ALVING, A S, JONES, R, Jr, WHORTON, C M, PULLMAN, T N & EICHELBERGER, Lillian. **The Chesson Strain of *Plasmodium vivax* Malaria. II. Relationship between Prepatent Period, Latent Period and Relapse Rate** *J Infect Dis* 1947, May-June, v 80, No 3, 228-36, 5 figs

These observations were carried out in a non-endemic area, only presumably susceptible white males were involved, and observations were restricted to primary attacks and first or second relapses, which were promptly treated by a variety of drugs.

In persons infected with the Chesson strain of *P vivax*, by the bites of 10 infected mosquitoes, the relapse rate was high when the prepatent period was short. Persons with a prepatent period of 14 days or less had a relapse rate of 96 per cent after treatment of the primary attack. When the prepatent period was 15 days or more the relapse rate was 58 per cent. One hundred and eleven cases were studied. The relapse rate after treatment of the first relapse was 85 per cent in patients who had had a short prepatent period, and 37 per cent in those who had long prepatent periods (82 cases observed).

The duration of the first latent period after treatment of the primary attack was usually short if the prepatent period had been short, 89 per cent of such

patients relapsed within 30 days, whereas only 46 per cent. of the relapses that occurred after long prepatent periods did so within that 30 days.

When the preceding latent period was under 30 days the relapse rate after treatment of the attack was 85 per cent. whereas it was only 52 per cent. when the latent period had exceeded that period (109 observations). The length of succeeding latent periods was positively correlated to the length of preceding latent periods.

The 30-day dividing line is not applicable to patients who have been treated previously with atabrin or with other drugs that persist in the body.

The relative importance of virulence and immunity as factors determining the severity of infections cannot be evaluated in such studies as these. The number of sporozoites injected is an important factor. If this be very high, the prepatent period is usually short.

Norman White

WHORTON, C. M., YOUNT, E., JR., JONES, R. JR., ALVING, A. S., PULLMAN, T. N., CRANGE, B. JR., & ESCHELBERGER, Lillian. The Chesson Strain of *Plasmodium vivax* Malaria. III. Clinical Aspects. *J. Infect. Dis.* 1947 May-June, v. 80 No. 3 237-49 8 figs. [23 refs.]

This is a note of the clinical aspects of 195 sporozoite-induced and 123 trophozoite-induced cases of *P. vivax* malaria, Chesson strain. There were very few prodromata. Irregular remittent fever was observed during the first few days in both types of infection. In sporozoite infections, 80 per cent. of patients with primary attacks had quotidian fever; the incidence of quotidian fever was lower in relapses. In trophozoite-induced infections early quotidian paroxysms usually changed to tertian as the disease progressed. Chills were not usually experienced during initial remittent fever. In general the signs and symptoms appear to have differed little, if at all, from those generally seen in *P. vivax* malaria.

Norman White

COOPER, W. C., COATNEY, G. R. & RUCK, D. S. Studies in Human Malaria. V. Homologous Strain Superinfection during Latency in Subjects with Sporozoite-Induced *Vivax* Malaria (H. Elizabeth Strain). *Amer. J. Hyg.* 1947 July v. 46 No. 1 141-8, 1 fig. [20 refs.]

Fifty million homologous-strain *P. vivax* parasites were injected intravenously into 15 patients, 4 months after their original infection with mosquitoes. The long-term latency in ten of these patients had resulted from complete suppression of early attacks by quinine (mepacrine) or NIH 204 (SN 1796). In the other five patients latency followed treatment of early attacks. All the recipients except one developed prompt and severe attacks of malaria as the result of this superinfection. Neither by prepatent periods, incubation periods, densities of parasitaemia at onset of fever, rates of increase of parasitaemia, peak parasite densities, fever peaks nor responses to therapy could any consistent difference be found between the quinine group, the NIH 204 group, the otherwise treated group or in two patients who had experienced no prior sporozoite-induced infection. The one failure to secure a definite superinfection was in a patient who exhibited persistent patent parasitaemia after an inadequately treated early relapse. Treatment of all superinfections was begun on the 11th day after inoculation. The patients who developed superinfections later developed delayed attacks apparently resulting from the original sporozoite infections. These late attacks were contemporaneous with those of fifteen other patients who had received sporozoite infections at the same time but had not had superinfections.

Norman White

Ross, P Sub-Tertian (Malignant Tertian) Malaria in Europeans *East African Med J* 1947, Aug, v 24, No 8, 278-88

The author has over 20 years' experience in treating subtertian malaria amongst Europeans in Kenya. Most of his service has been in the Kisumu and Mombasa districts, and he has treated over one-thousand patients in hospital and several thousands as out-patients.

He considers that the "protean" nature of subtertian malaria has been greatly exaggerated and that an acute attack is a clear-cut entity and is comparatively easily diagnosed. In a patient coming from a malarious district, having a temperature, where no antimalarial drug has been given, competent examination of the blood repeated at intervals of 12 to 24 hours will prove the presence or absence of the disease almost invariably. If such drug has been given, two courses are open: either the drug is continued in full doses for a week—failure to respond being almost certain evidence that the condition is not malaria—or it is stopped and repeated blood examinations are made (the ideal course). [This of course is safe only when the patient is under close observation.]

It is not believed that, under proper observation, harm ever results from delaying treatment, except in children. The author has never seen a case of coma or convulsions with a negative blood slide. The habit of necessarily ascribing all of a patient's symptoms to a subtertian infection found in the blood is a bad one, and moreover textbooks do not sufficiently discriminate in their descriptions of the disease as it affects Europeans, Asians and Africans. In Europeans, dysenteric symptoms due to malaria are thought to be very rare, and even if parasites are found, the stools should be carefully examined in such cases. [Malaria and amoebic dysentery not infrequently co-exist in certain districts.]

The author has found that the disease rarely simulates appendicitis, although he has met with a proved case in which an appendix abscess subsequently developed. Chronic subtertian malaria is considered usually to be the result of repeated reinfections and is met with in Europeans living in an area so malarious that reinfections are unavoidable. Such patients treat themselves with quinine or mepacrine (usually in quite inadequate doses and irregularly), get into a state of "uneasy equilibrium" and are prone to blackwater fever.

Finally, the ultimate diagnosis of malaria rests with the microscope.

The newcomer is advised that particular note should be taken of the district from which the patient comes. [Very sound advice in East Africa.]

Areas are divided into Group I, townships such as Kisumu and Mombasa, where residents are liable to occasional infections only, and Group II, hyper-endemic areas where repeated reinfections are liable to take place. Care should be taken in ascribing unusual symptoms to malaria.

Subtertian malaria has very little tendency to relapse if it is properly treated, so-called relapses being nearly always due to reinfections. When malaria does relapse after the patient has left the endemic area the probability is, as the author points out, that there is a coincident benign or quartan infection.

All will admit that a great change has occurred in the therapeutics of malaria in the last 20 years. In the past, undoubtedly, too long and heavy courses of quinine were recommended, probably because relapse and reinfection were confused. The author has found that a course of 15 to 20 grains of quinine a day for 5 days and then 10 grains daily for a week, or of mepacrine 0.3 gm daily for 5 to 7 days, followed by a similar course for a week, is quite sufficient. His own last attack in 1942 was treated with only 80 grains of quinine and there was no suggestion of a relapse.

In a series of cases where quinine and mepacrine were given to alternate patients little difference in results was found but it was noted that the latter was rather slower in its action and that parasites disappeared more slowly from the peripheral blood. Two cases of psychosis were noted after ordinary doses of mepacrine and it is thought that the larger doses now sometimes recommended are unwise no benefit was found from giving the two drugs together and no treatment brought about disappearance of symptoms in less than 5 days in first attacks. Paludrine was not tried.

In chronic (usually recurrent) malaria, failing removal from the endemic area, each attack should be treated as it arises and a suppressive dose of mepacrine given daily.

Cerebral malaria has been found to be rare in European adults having efficient treatment, although it has been seen. It occurred most commonly in Group 2 cases, who have become careless. Blackwater fever usually occurred in Group 2 cases it was never seen in a first attack and followed as a rule irregular taking of quinine and also mepacrine. In contrast to cerebral malaria, it not uncommonly supervened in patients in hospital under treatment.

For cerebral malaria, it is thought that 5 grain doses of quinine given intravenously and repeated is the best treatment, although mepacrine has been used. In blackwater no specific was found, and sodium luminal in large doses intramuscularly did not reduce the mortality.

Malaria is a much more dangerous illness in children, especially infants, and here it does tend to be more "protean" in character. Withholding treatment while awaiting the result of blood examination is not recommended and it is important to give quinine or mepacrine, preferably by injection, at once in any suspicious case. Cerebral symptoms may develop very quickly but the treatment of this complication is more satisfactory than in adults. In infants, the onset may be very insidious. [In the reviewer's experience this is especially true in breast fed infants.]

The author considers the term *malignant malaria* is a bad one and unjustified. An occasional attack of subtertian malaria, if properly treated, makes little difference to the patient's general health. [The term malignant is probably a relic of bygone days when mosquito control was almost nil, the condition often not recognized or badly treated, and repeated reinfections frequent. In these circumstances, it was a very fatal disease and blackwater was common for instance in the Gold Coast, where circa 1830 some 30 per cent. of new arrivals died in their first year mostly from malaria and black water.]

Although no one is probably absolutely immune to this infection some appear to have a higher resistance than others, although here the degree of personal anti-mosquito prophylaxis must be taken into account. Those leading the quiet life usually suffer less than those who are constantly out at night.

Those living under Group 1 conditions are not advised to take any drug prophylaxis, those under Group 2 to take a daily suppressive dose of mepacrine. Paludrine has not been tried by the author.

[This is such an excellent paper and so full of practical experience that the reviewer hesitates to make any criticisms. It is, however suggested that —

1. The author tends to underestimate the protean manifestations of malaria.
2. In many cases parasites are extremely hard to find within the first 2 to 3 days of illness.
3. Cerebral malaria does occur with a negative blood slide, even in adults.
4. Malaria tends to simulate the symptoms but not the physical signs of other diseases, e.g. pain in the right iliac fossa, vomiting, possibly tenderness, but no rigidity and no diminution of peristaltic sounds.]

C. F. Shelton



HERNBERG, C A **Myocardial Affection in Malaria Tertiana** *Acta Med Scandinavica* 1947, Nov 5, v 129, No 2, 132-41, 6 figs

In 1944, the author saw 9 cases of myocarditis among 596 people suffering from "malaria tertiana" [presumably benign tertian] In three of these, electrocardiographic changes were uncertain, in the other six, which are described in detail, such changes did occur in some degree and included a reversible lowering of the S-T lead and a negativity of the T-wave at times, the P-wave was changed

The patients were all men between 20 and 40 years three were farmers and one each was a stone-worker, a chauffeur and a sausage maker [and were thus all manual workers, for the most part in moderately heavy occupations] Malaria parasites [presumably *P vivax*] were found in the blood of each patient, on admission in 3 cases, and, in the others, on the 24th day, the 4th week and not "till a relapse occurred"

The nature of the myocardial lesion was manifested by the presence of praecordial oppression, tachycardia, changes in the heart sounds and an increased sedimentation rate In only one case did permanent cardiac damage and insufficiency ensue

The myocardial condition was seen, on an average, 43.5 days after the first attack of fever, and usually about a fortnight after the end of antimalarial treatment The pathology of the condition is discussed and it is suggested that it may have been caused by blocking of the capillaries by malarial elements No other cause was found the patients were previously healthy soldiers on active service

On the basis of the return to normal of the sedimentation rate, the disappearance of symptoms and stabilization of the Ecg, the active process in the heart appeared to occur over a period of 3-10 weeks

H J O'D Burke-Gaffney

CHEN, J H & WU, Y K **Transfusion Malaria and its Prevention by Quinine Therapy** *Chinese Med J Shanghai* 1946, Nov-Dec, v 64, Nos 11/12, 309-14

This report is based on 233 blood transfusions performed in the Chungking General Hospital The blood was given to the patients immediately after withdrawal from the donors It was difficult to get a reliable past history of malaria from these donors One hundred and thirteen patients were given transfusions without quinine prophylaxis Twenty-one developed malaria, 18 *P vivax*, 3 *P falciparum* Five of the 21 patients had a history of past malaria moreover the hospital is in an endemic malaria area

The second group of 120 patients were given quinine by mouth as soon as possible after the transfusions, 0.3 gm four times daily for from 5 to 7 days None of these patients developed malaria in hospital

The authors recommend the routine use of quinine after blood transfusions in an endemic area such as Chungking

Norman White

ROGERS, K B **Quartan Malaria transmitted by Blood-Transfusion Report of a Case** *Lancet* 1947, Nov 8, 688-9, 1 chart [16 refs]

It is recognized that malaria may be transmitted by blood-transfusion and it has been suggested that persons who had lived in tropical or sub-tropical areas should not be used as donors if others can be found [this *Bulletin*, 1940 v 37, 362, 456] This question has become more obtrusive now that many ex-service persons are potential donors, and the author records a case which emphasizes the risk of using donors who have visited malarious areas, without having had clinical manifestations of the disease

A young primipara, who had never travelled outside the county of Durham, received an antepartum transfusion of blood on March 8th 1948 this consisted of 2 pints of homologous (A) blood which had been stored for 3 days. She was discharged without incident, and was delivered of a healthy full-term child on March 14th at the same hospital. Except for one day of pyrexia, her post-partum was normal and she went home on March 24th.

Seven or eight weeks after the transfusion, she felt run down, sweated freely at night and eventually entered the county post natal convalescent home on June 15th, with a cold. On 18th she had a slight rigor which was repeated on 19th, 22nd and 25th. Between the rigors, she felt well. On 25th, typical quartan malaria parasites were found in her blood. By this time, the patient was pale and had an easily palpable spleen and liver.

Blood examination which was very full and is recorded in detail, revealed, *inter alia* 3,600,000 red cells per cmm. 10.5 gm. Hb per 100 cc., and a blood sedimentation rate of 53 mm. in 1 hour (Wintrobe).

Agglutination tests and blood culture were negative. The patient was treated with quinine and mepracrine to which she responded rapidly. Up to the age of 5 months the child has shown no evidence of malaria.

There were two blood donors concerned. One had been on a cruise and had landed at Algiers for a few hours: no parasites were found in her blood. The second donor was a ship's engineer who had been to Aden, Abadan and Basra for five months in 1939. He had never had malaria (but several members of the crew had 3-day malaria on the homeward voyage). On his return to Britain in the summer of 1939 he had bouts of feeling cold for short periods, and would go to bed for an hour during the day. He had not been out of England since and had no illness except this during a local epidemic.

Examination of concentrated centrifuged blood from the second donor by the author's technique [this Bulletin 1946 v 43 362] revealed the presence of a definite male quartan gametocyte.

On July 4th, blood from both donors was injected into two patients with G.P.I. who belonged to blood-group A: no evidence of malaria has yet appeared in the patient who received blood from the first donor. The patient given the blood of the second donor developed malaria on August 5th. It is noted that although this donor was an active malaria carrier his blood-sedimentation rate was not raised.

The author discusses the incidence of malaria transmitted by blood transfusion and surveys the relevant literature. He notes that the malaria transmitted by donors who have been absent from malarious areas for many years are nearly all quartan infections, though he mentions two benign tertian cases in the literature in which the donors had carried parasites for 3 and 10 years. He points out with SMITH [this Bulletin 1944 v 41 1002] that quartan malaria is often no less common than the other varieties, and that it may be latent in persons from the tropics who act as donors. LÖNNER and NERHÖJER [ibid., 91] have, however, shown that, when plasma is used, the risk of transmission of malaria is negligible: the author therefore suggests that persons who have been resident in malarious areas should not be bled for the production of whole blood for the purposes of transfusion.

H. J. O'D. Burke-Gaffney

WINKLER, C. W. F. Quinine Injections in Malaria. *J Trop Med. & Hyg* 1947 Oct. v 50 No 10 201-3.

The author considers that quinine will still hold its place against the newer synthetic antimalarial remedies for a considerable time.

Parenteral administration of quinine is held to be justified only (1) When for some reason its oral use is impossible (2) to make sure that the drug is

actually being absorbed, (3) in very severe cases (e.g. cerebral malaria) when the quickest possible action is necessary.

In (1) and (2), intramuscular, and in (3) intravenous, injections should be given.

Until recently, quinine dihydrochloride was the compound of choice, but as the author points out, the acidity (pH-3.5) of the solution tended to cause pain and necrosis of tissue, the latter predisposing to infection and abscess formation even after the greatest aseptic precautions.

The author recommends the less soluble hydrochloride salt according to the following prescriptions (for intramuscular use) —

Quinine hydrochlor	8 grains (0.5 gm)
Urethane	4 grains (0.25 gm)
Aq. dest. ad	1 ml
or Quinine hydrochlor	4 grains (0.25 gm)
Antipyrin	2 grains (0.125 gm)
Aq. dest. ad	1 ml

These solutions are nearly neutral and pain and necrosis are reduced to a minimum. The pH of these solutions may be raised to that of the tissues (pH 7.2) by adding a small amount of quinine base, this being the method used in the preparation of the German compound "Solvochin".

The following prescription gives a solution very nearly approaching the alkalinity of the body tissues

Quinine hydrochlor	45 grains (3 gm)
Antipyrin	30 grains (2 gm)
Sol. hydratis sodi norm	0.75 ml
Double-distilled water to	10.0 ml

This is for intramuscular injection only. It may be diluted up to three times its original volume without causing precipitation of quinine, it is not suitable for intravenous use. [No indication is given of the single dosage of this prescription which should be used.]

For intravenous use, the first two prescriptions should be diluted ten times and not more than 8 grains given at one time. Injections must be given slowly, one-tenth of the dose every minute. [The use of quinine hydrochloride might with advantage be tried out more extensively, especially for intramuscular injection. The advantages are that the injections are painless, necrosis of tissues is insignificant and therefore danger of sepsis is greatly reduced.]

C. F. Shelton

1. WINCKEL, C. W. F. The Malaria Patient and Quinine. *J. Trop. Med. & Hyg.* 1947, Nov., v. 50, No. 11, 219-20.
2. J. TROP. MED. & HYG. 1947, Nov., v. 50, No. 11, 211-12. The Route and Dosage in Antimalarial Therapy.

The author doubts whether mepacrine, paludrine and chloroquine can yet be issued wholesale with safety to the populations of tropical malarious countries in the same way in which quinine has been sold and distributed by various governments.

It is remarked that British and American authorities have tended to recommend larger daily doses of quinine than continental ones. The former generally advocate a daily dose of 30 grains or so. Thus MAEGRAITH (*Practitioner*, 1946, v. 157-81) recommends 30 grains a day for two days followed by 20 grains daily for the next five, relapsed cases are treated with 30 grains combined with 30 mgm. pamaquin, daily for ten days, the quinine is given either as a

solution of bisulphate or as tablets of the hydrochloride or bihydrochloride. The author notes that the bisulphate contains 59 per cent. of quinine base, the hydrochloride and bihydrochloride 82 per cent.

*P. falciparum* infections may require more quinine than those due to *P. vivax* first attacks need larger doses than relapses, and a large discrepancy may exist on account of varying strains of plasmodia.

In the Netherlands East Indies, including parts of New Guinea, a daily dose of 22 grains of bisulphate or hydrochloride was found sufficient even for bad cases of *P. falciparum* infection, and in treating *P. vivax* a dosage of 15 grains was seldom exceeded. In 1832 in Java, Lichtenstein found that 9 grains daily of hydrochloride acted as well as 18 grains.

In Holland, the following treatment of *P. vivax* infections has been found successful—12 to 14 grains of quinine sulphate plus 45 to 54 mgm. pamaquin naphthoate (equal to about 30 mgm. pamaquin) are taken daily in 3 or 6 equal doses for 10 to 14 days. The author's point is that a small amount of quinine appears to be effective and there appears to be no reason why moderate doses of this drug should not work as efficiently in other parts of the world as in Holland and the East Indies.

[The reviewer believes it to be now generally held that excessive and too prolonged dosage with quinine is unnecessary and may be harmful—our experiences in Macedonia in 1917-18, when enormous doses of the drug were often given to malaria patients.]

ii. Two opposing views are put briefly in an editorial in the same *Journal*

(1) The surest way of obtaining the full action of quinine is by intramuscular injection, and this should be the routine in treatment of malaria.

(2) Intramuscular injection is unnecessary and dangerous and little short of malpraxis.

The view expressed in the editorial is that the parenteral route is seldom necessary and when it is, intravenous quinine is preferable to intramuscular but if the former is contraindicated the latter route may be used.

As pointed out by WINCKEL (above) the neutral hydrochloride salt is preferable to the highly acid and irritating bihydrochloride. The low solubility of the former may be overcome by addition of urethane and the resulting solution is nearly painless and non-irritating on intramuscular injection.

The danger of intravenous atabrin (mepacrine) is thought to have been exaggerated, but intramuscular injection seems to be just as effective, and the same applies to the newer synthetic drugs. As pointed out above there is a marked difference in the quinine base content of the various salts of quinine. During the recent war there has been a tendency to re-introduce the prescribing of larger doses of quinine, one possible reason being that the amount prescribed was not actually being taken.

Investigations with the synthetic antimalarial drugs led to the practice of loading—the first few doses so as to reach the necessary blood concentration in the shortest possible time, but with quinine this is not necessary. The writer of the editorial under review is uncertain whether the minimal doses of quinine recommended by Winckel will be generally adopted.

[The evil reputation of intramuscular quinine in the past has probably arisen from the experience of those working in parts of the world where *C. leish* and other spore-bearing organisms are excessively common. Autoclaved sealed ampoules of quinine as supplied by any reliable firm of wholesale chemists are practically always sterile but difficulty may arise in the sterilization of needles and syringes, and the most careful precautions should be taken in this connexion.]

C. F. Skilton

GHOSH, B N & GHOSH, T K Chemotherapy of Malaria with special reference to Paludrine. *J Indian Med Ass* 1947, May, v. 16, No 8, 267-9

The authors discuss briefly the morbidity of malaria, the common anti-malarial drugs and the introduction of Paludrine they then give a brief [but not very clearly stated] description of the biology of malaria parasites and the conceptions of the exo erythrocytic phases, together with their therapeutic implications

The authors then report the use of paludrine by them in 50 cases of malaria, which could be followed up and supervised for a prolonged period Their results are summarized as follows —

Average daily dose	Total dose for the course	Day of disappearance of fever	Day of disappearance of parasite	Relapse checked with periodic use
100 mg to 200 mg	300 mg to 700 mg	2nd day (90 per cent)	2nd/3rd day (80 per cent)	90 per cent

It is stated that the drug is generally given in tablets of 100 mgm twice a day for two or three days until the fever subsides except for slight nausea, "which is not felt when taken with a glass of water", no toxic symptoms were observed, no untoward effect was observed when the drug was used in the case of two pregnant women

"In malignant malaria it will cause definite cure But relapses may occur in benign tertian after a few days when it may be used twice a week for 3-6 months to stop it

The authors discuss the estimated quinine needs of India and compare them with the economic advantages of paludrine

They finally draw a number of conclusions regarding paludrine which accord in general with those of many other observers but these conclusions do not all follow from the somewhat scanty experimental records provided in the paper [The authors do not give details of their cases or the types of malaria of which they consisted conclusions regarding prophylaxis and suppression are drawn without provision of experimental evidence on which to support them See also this *Bulletin*, 1948, v 45, 34-6]

COOPER, W C & COATNEY, G R Studies in Human Malaria III The Therapeutic Effect of a Phenanthrene Amino Alcohol, NIH-204 (SN-1796), in Vivax, Falciparum, and Quartan Malaria *Amer J Hyg* 1947, July, v 46 No 1, 119-31 2 figs

The chemical formula of NIH-204 is 9-(2-diamylamino-1-hydroxyethyl)-1, 2, 3 4-tetrahydrophenanthrene hydrochloride This report summarizes the treatment of 66 malaria attacks in 47 patients undergoing therapeutic malaria in a mental hospital Fifty-one attacks were due to *P vivax* In these infections 0.5 gm of NIH-204 or more a day for 6 days relieved the clinical attack and reduced parasitaemia to subpatent levels in all but one instance Relapses occurred after treatment of all sporozoite-induced early attacks, regardless of dosage Prompt relapses (4 to 27 days after treatment) appeared after all early attacks treated with 0.25 gm daily and in the majority treated with 0.5 gm daily but after only 3 of 16 attacks treated with 0.9 gm daily relapses in the 13 other cases were delayed 153 to 273 days

Thirteen attacks due to *P falciparum* were treated with NIH-204 The doses were 0.96 gm daily in 10 cases, 1.5 gm daily in 3 cases In all but one

instance there was parasite and clinical response. The clearance of parasites and subsidence of fever were generally slow in primary attacks. Early relapses occurred after 5 of the 8 primary attacks and after 2 of 4 first relapses.

Two blood-induced *P. malariae* infections were treated with NIH-20; parasites disappeared and fever subsided in both. There was no relapse during 4 years of observation.

Symptoms of intolerance noted were lowering of the threshold of pilomotor stimulation in most cases, marked but asymptomatic bradycardia in 42 cases, difficulty in passing urine in 8 cases, and microscopic haematuria in 17.

At the doses used, which were near the limit of tolerance, NIH 20 is certainly no better than quinine and definitely inferior to mepacrine in the treatment of *P. vexans* malaria. It is inferior to both drugs in the treatment of *P. falciparum* infections.

Norman White

DEGOUT P & SCHNEIDER, J. Traitement curatif du paludisme par divers sels du 3-méthyl-4 (diéthylaminopentyl) amino-7-chloroquinoline (nivaquine) [Curative Treatment of Malaria with various Salts of 3-Methyl-4 (Diethylaminopentyl) Amino-7-Chloroquinoline (Nivaquine)] *Bull. Soc. Path. Exot.* 1947 v 40 Nos. 1/2, 14-17

Three salts of nivaquine the composition of which is indicated in the title to this paper have been tested in the treatment of malaria in Tunisia: a methylene bis-oxynaphthoate, Nivaquine M; a resorcin-carbonate, Nivaquine R; a dichlorhydrate Nivaquine C. Nivaquine was formerly known as Sontoquine.

More than 150 patients have been treated with Nivaquine M. The average dose was 0.6 gm. a day for 5 days. Fever was controlled in 36 hours and schizonts disappeared from the peripheral blood in 48 hours.

Nivaquine R was used in the treatment of only 17 patients. The results were very much less favourable than those obtained with Nivaquine M.

Nivaquine C was much more active in the treatment of malaria than either of the two other preparations. More than 200 patients have been treated with it. The daily dose in cases of average severity was 0.3 gm. A daily dose of as little as 0.08 gm. is sufficient to arrest the attack. 0.1 gm. of quinine is necessary to secure the same result. Patients treated for 5 to 7 days are always afebrile at the end of 36 hours: no relapses were noted in the several weeks during which the patients were under observation. All doses in this paper are doses of base.

Norman White

KING, H. & TOWKIN, Isabel M. Antiplasmodial Action and Chemical Constitution. Part VIII. Guanidines and Diguanides. *J. Chem. Soc.* 1946, Nov. 1063-6

HARRER, H. J. & WRAOQ, W. R. Contributions to the Chemistry of Synthetic Antimalarials. Part IV. Hydroxyl Hydrolysis and Radical Exchange Reactions of N-Substituted Phthalimides in relation to the Constitution of the Antimalarial R.61. *J. Chem. Soc.* 1947 Oct. 1331-7

BARFORD, P. R., CURD, F. H. S., HOGGARTH, E. & ROSE, F. L. Synthetic Antimalarials. Part XXI. 4-Arylamino-8-Ambisalkylaminoquinolines. Further Variations. *J. Chem. Soc.* 1947 Oct. 1354-64

DE MEILLON B & THORP, J M The Inhibition of Growth of Larvae of *Aedes aegypti* by certain Anti-Malarial Drugs *South African J Med Sci* 1947, Jan, v 12, No 1, 33-8

In this paper are recorded the results of experiments which demonstrate the inhibition of the growth of the larvae of *Aedes aegypti* by quinine and atabrin [mepacrine] and the reversal of this inhibition by dietary means. This work has followed on that of MADINAVEITIA [this *Bulletin*, 1946, v 43, 1011], who found that antimalarial drugs inhibit the growth of *Lactobacillus casei*, and HELLERMAN *et al* [*ibid*, 1947, v 44, 400], who showed that adenylic acid could reverse the inhibitory effect of quinacrine on the growth of *Plasmodium lophurae*. The object of this paper was to examine the relation of these effects of antimalarials to living systems other than micro-organisms.

In an adequate medium containing minimal quantities of brewer's yeast and a vitamin mixture, reversal of inhibition was attained by increasing the yeast fivefold or by the addition of the water-soluble fraction of yeast, definite reversal did not follow an increase in concentration of the vitamin content, namely thiamin chloride, riboflavin, pyrodoxin, pantothenic acid and nicotinic acid.

R Ford Tredre

GOLDBERG L & DE MEILLON B Further Observations on the Nutritional Requirements of the Larva of *Aedes aegypti* L *Nature* 1947 Oct 25, 582-3, 1 fig [See also DE MEILLON & THORP above Detailed findings will be furnished later]

PACKER, H Experimental Field-Type Suppression with SN 7618 (Chloroquine) SN 8137 and SN 12,837 (Paludrine) *J National Malaria Soc* 1947 June v 6, No 2, 147-54

These observations were carried out on white neurosyphilitic patients, without a previous history of malaria, who had been admitted to hospital for malaria-therapy. The McCoy strain of *P vivax* and the Costa strain of *P falciparum* were used, and insectary-bred *A quadrimaculatus* was the vector.

Twelve patients received weekly doses of SN 8137, from 0.125 to 0.5 gm. without a priming dose. They were given mosquito inoculations of *P vivax* on three alternate days of the first week, the first weekly dose of drug being given the day before the first inoculation. The weekly dose of drug was continued during three consecutive weeks following the week of inoculations. The minimum effective weekly suppressive dose was found to be between 0.125 and 0.25 gm. No break-through occurred when the higher dose was given. Equivalent doses of SN 7618 (chloroquine) were not so effective against *P vivax* break-throughs occurred with 0.25 gm weekly. If, however, a priming dose of double the weekly maintenance dose was given a week before the week of inoculations the results obtained were similar to those obtained with SN 8137. The minimum effective dose of paludrine against *P vivax* was not determined but observations on four patients showed that the amount of the drug required against *P falciparum* paludrine was found to exercise suppressive action comparable with that of chloroquine in doses three times as large. *P falciparum* infections require higher doses of either drug for effective suppression than do *P vivax* infections.

Paludrine given on any day between the first and fifth days, inclusive, after *P falciparum* mosquito inoculation gives protection. If given on the sixth or seventh days infection breaks through. This confirms Fairley's observation

that palabrine is a true causal prophylactic in *P. falciparum* malaria and is more active against pre-erythrocytic forms than against the erythrocytic stages of the parasite.

Norman White

- i. COATNEY G. R., COOPER, W. C., YOUNG M. D. & McLENDON S. B. Studies in Human Malaria. I. The Protective Action of Sulfadiazine and Sulfapyrazine against Sporozoit-induced *Falciparum* Malaria. *Amer J Hyg* 1947 July 1 48 No. 1 84-104. [17 refs.]
- ii. — — — — — BURGESS, R. W. & SMARR, R. G. II. The Suppressive Action of Sulfadiazine and Sulfapyrazine against Sporozoit-induced Vivax Malaria (St. Elizabeth Strain) *Ibid.* 105-18 1 fig. [29 refs.]
- iii. — — — — — & — — — — — IV. The Suppressive Action of a Phenanthrene Amino Alcohol, NIH-204 (SN 1796) against Sporozoit-induced Vivax Malaria (St. Elizabeth Strain). *Ibid.* 132-40 2 figs.

i. I.—These investigations were carried out in 1942-43. For the *P. falciparum* investigation, the subjects were selected from white and Negro male patients in two large mental hospitals. The McLendon strain of *P. falciparum* was used. This was isolated from a patient in South Carolina in 1940. Insectary-reared *A. quadrimaculatus* were used as vectors. Sulphadiazine and sulphapyrazine were given in 0.5 gm. tablets. In all but one test administration of the drug was begun before exposure to infection. The tests involved 75 treated and 36 control subjects. Sulphadiazine in doses 1-12 gm. a day continued for 48 hours after exposure with blood concentrations over 20 mgm. per 100 ml. did not act as a causal prophylactic of *P. falciparum* malaria: the prepatent and incubation periods were, however, doubled. Four grammes daily for 6 days after exposure, or 2 gm. daily for 5 days or 10 days, produced delay of patent infection. Four grammes daily for 11 days after exposure prevented infection in 4 of 5 patients. Four grammes daily for 42 days after exposure protected all of 10 patients. 2 gm. daily for the same period 9 out of 10. 1 gm. daily for the same period protected 8 out of 10. 0.5 gm. daily for the same period prevented patent parasitaemia and clinical attacks in 3 of 5 subjects, but borderline clinical symptoms occurred. The minimum blood concentration of sulphadiazine associated with suppression was approximately 1.1 mgm. per 100 ml.

One-half gramme of sulphapyrazine daily for 42 days after exposure gave results similar to those given by the same dose of sulphadiazine.

As a suppressive of *P. falciparum* malaria sulphadiazine possesses no advantages over atebirin (mepacrine).

ii. II.—Similar observations were carried out on white male patients infected with the St. Elizabeth strain of *P. vivax*. Sulphadiazine 3 gm. daily for 2 days before and 42 days after infective mosquito bites, did not prevent infection in any of 10 patients. Mean minimum blood concentrations of over 5.0 mgm. per 100 ml. were suppressive. In 4 patients, malaria appeared 9 to 11 months after infection. With smaller doses the majority of patients developed clinical attacks while receiving treatment. Sulphapyrazine, in daily doses of 1.0 and 0.5 gm., was similarly ineffective. With these drugs, *P. vivax* malaria is far more difficult to suppress or prevent than is *P. falciparum* malaria. Both drugs are poor suppressants of the strain of *P. vivax* used, compared with either quinine or mepacrine.

iii. IV. In this study 30 white patients were observed. The suppressive action of NIH 204 (SN 1796)—a phenanthrene amino-alcohol—was compared with that of mepacrine against *P. vivax* infection. There were ten patients in each of the two groups and ten controls who received no protective medication. NIH 204 was given in capsules containing 0.15 gm. of the hydrochloride.



(91.2 per cent base) Quinacrine [mepacrine] dihydrochloride was given in standard 0.1 gm tablets. Each man was bitten by from 3 to 7 infected mosquitoes on each of 3 days spaced evenly over a week. NIH-204 0.3 gm daily, for 2 days before, 7 days during, and 28 days after the week of infection, effectively suppressed *P. vivax* malaria, as did quinacrine hydrochloride 0.1 gm daily commencing 8 days before the week of infection. All of the subjects developed delayed primary attacks 6 to 10 months after exposure to infection. NIH-204 is not recommended for the field suppression of malaria because of annoying side-actions that accompany its use, and because better suppressants are available. The side-actions were lowering of the threshold of pilomotor stimulation, slowing of the pulse, difficulty in urination, and microscopic haematuria.

MISSIROLI, A. Riduzione o eradicazione degli anofeli? [Reduction or Eradication of Anophelines?] *Riv di Parassit* Rome 1947, June-Sept, v 8, Nos 2/3, 141-69, 9 figs. English summary (7 lines) Norman White

In the autumn of 1943 there were large inundations of parts of the Tyrrhenian seaboard of Italy owing to the war. Breeding of mosquitoes increased and, in addition, the percentages of *Anopheles maculipennis labranchiae* rose to nearly 100 per cent in some areas. The result was a great increase in the incidence of malaria. A new method of attack on this old problem was attempted with the aid of funds and equipment from UNRRA and other sources. Instead of anti-larval treatments and other measures, reliance was placed on anti-adult spray-painting of houses and animal sheds with DDT. The method has proved so successful that a five-year plan has been started to eradicate malaria from Italy. The country falls into four distinct regions differing in their particular malaria problems. (I) The northern plain of Lombardy has only local patches of malaria, due to *Anopheles maculipennis atroparvus*. (II) The coastal region of the northern end of the Adriatic has malaria spread by *A. sacharovi*. (III) The central part of Italy suffers from malaria spread by *A. m. labranchiae* which occurs along the coast of Tuscany and Lazio at places below 300 m above sea level. (IV) The southern part of Italy as well as Sicily and Sardinia constitute the most difficult problem, for malaria spread by *A. m. labranchiae* is common everywhere in regions below 1,000 m above sea level.

The aim of the plan is to treat all houses in the malarious patches of zones I, II and III in the first year, in the second year, to deal with the western and in the third year the eastern halves of zone IV. Results of work completed so far are given in graphs which show the monthly statistics for certain areas in 1945 (before DDT spraying) and in 1946 (afterwards). The graphs show striking declines in numbers of mosquitoes at catching stations, reported cases of malaria, positive blood films, deaths from malaria and also from all causes. The decline from all causes is due to the absence of a peak during the summer months in the year of DDT spraying. This appears to be due not so much to the effect on malaria as to a reduction of enteric diseases consequent on the widespread destruction of houseflies achieved by the DDT. Figures are also given of parasite rates and spleen indices for March 1946 and March 1947.

The author briefly discusses the possibility of eradication of mosquitoes and remarks that further judgment can be made at the end of an eradication campaign now in progress in Sardinia. He concludes that it would take fifteen years at least to do such a thing in Italy itself and would be exceedingly costly. On the other hand the use of DDT spray-painting was easier and cheaper and affected flies and other parasites as well as mosquitoes. An indication of a race

of flies with unusual resistance to DDT complicated the picture, but it appears that they may be attacked with other similar insecticides. J. R. BURRIS

PUTNAM, P & HACKETT L. W. An Appraisal of Malaria Reduction in Albania, 1929-1938. J. National Malaria Soc. 1947 June, v 6 No 2, 131-46 7 figs.

Malarial surveys and antilarval measures were started in Albania in 1929 by the Health Department of that country under the auspices of the International Health Division of the Rockefeller Foundation. Antilarval schemes were carried out in Tirana, the capital, Durazzo, its port, two inland towns, Elbasan and Berat, and the coastal town Valona. Kavaja, a coastal town just south of Durazzo was used as a control area. Annual surveys of school children, from 5 to 12 years of age, were made in February or March in all these towns.

*Anopheles sacharovi* is the important vector of malaria in the coastal plains where it breeds in the salty lagoons. *A. maculipennis maculipennis* and *A. m. subalpinus* were found wherever collections were made. *A. m. maculipennis* is a highland species. *A. superpictus* was found breeding extensively in the gravel beds of torrents during the dry summer. *A. maculipennis* (*maculipennis* and *subalpinus*) could be captured throughout the year but the high peak of prevalence occurred in June and July. *A. sacharovi* was prevalent in May, June and July, the shortness of the season being due to the increased salinity of the breeding grounds in the dry season. The seasonal prevalence of *A. superpictus* was irregular. The prevalence curve showed two peaks each year but specimens could be captured in any month.

At Tirana, where *A. superpictus* is the chief vector swamps were drained and all the river water was diverted above the town into a well-regulated irrigation system throughout the breeding season. At Durazzo the salinity of the lagoon was increased by admitting sea water at high tide. At Elbasan and Berat persimmon green was used extensively. At Valona filling and draining of swamps and lagoons were commenced but progress was slow.

The reduction in malaria is appraised by statistical methods. A reduction occurred in each of the protected areas, greatest in Tirana and Durazzo where permanent measures were possible. In Tirana the density of *A. superpictus* dropped sharply from 1932 to 1938 while that of *A. maculipennis* remained constant. In Elbasan and Berat the density of both species decreased. In Valona there was no decrease either in *A. sacharovi* captures or in parasite rates.

Norman White

I. AZIZ, M. Report on the *Anopheles* (Malaria) Eradication Scheme Karpas-Cyprus 1946. 67 pp. numerous graphs & charts & 33 figs. 1947. Nicosia Cyprus Govt. Printing Office.

II. — A Brief Account of the *Anopheles* (Malaria) Eradication in Karpas-Cyprus, 1946. J. Roy. Soc. Med. 1947 Sept., v 67 No. 5 498-509 3 figs.

i. The first stage of an attempt to eradicate anopheline mosquitoes and malaria from the island of Cyprus has been completed. The story is told in full in the first paper and summarized in the second.

The area chosen for the first season's work, 1st April to 16th November 1946 was the Karpas, the narrow tongue of land to the north-east of the island, the topography of which is described. It consists of about 450-500 square miles, but an additional inland protective area of some 250 square miles was also included and placed under control as a protection against *Anopheles* infiltration. In the rest of the island, the usual routine control, limited to 1½ miles around towns and villages, was continued. The population of both areas is 34,000.

living in 65 villages. The anophelines are *A. superpictus*, *claviger*, *sacharovi*, *algeriensis*, *marleri* and *hyrcanus*. *A. multicolor* occurs in other parts of the island. The three first named are known to be vectors of malaria, *A. superpictus* being responsible for 95 per cent of the rural malaria. In the island there is an average of 10,500 cases per annum with 18,000 in some years.

The recruitment of staff, organization of the eradication scheme and the duties of each member are described. When complete, the staff consisted of an executive officer and his assistants, a district officer, 2 headquarters inspectors, 4 section officers, 1 malaria technician, 2 field inspectors, 8 zone officers, 1 store-keeper, 3 clerks and between 75 and 80 labourers. The relationship between the workers had to be understood by all the checking and counter-checking of each other's work formed an essential part of the scheme and had to be undertaken without bad feeling or suspicion. Those accustomed to ordinary control work had to become "eradication-minded" and had to be continually impressed with the necessity for negative reports. The many difficulties encountered, and how they were overcome, are described in some detail. For example it was not possible to continue with routine treatment of vehicles travelling through the area until the public health legislation had been amended, and by that time it was too late to be effective. Some of the staff deserted for less hazardous occupations, but this was counteracted to some extent by the issue of free clothing, boots, soap and so on.

The area was divided into 51 blocks of 10 to 30 square miles each, though the sizes had to be adjusted in the light of experience as the work progressed. In each block were 12 plots and one labourer was expected to do one plot per day. Blocks were grouped into 10 zones and the whole peninsula into 4 sections. Most attention was given to breeding places. These were dotted over many places. Some of them were very difficult to reach. At first, DDT residual spraying was not done but 'ordinary insecticide' was used in houses, stables, etc. as it was not possible to treat buildings properly because there were many rooms to which the operators were not admitted, later, a "light DDT spray" was used in adult resting places as the weather got colder.

The materials used were against larvae, 8,416 gallons of 4 to 5 per cent DDT in gas oil (fuel oil), against adults, 160 gallons of 3 per cent DDT in gas oil, 'ordinary insecticide' [pyrethrum] 168 gallons, 193 larvicide sprayers (lengthened fit guns) and 84 standard fit guns, all made locally. The cost to 31st October 1946 was £12,000. Monthly progress was recorded in tables and on maps until finally it was possible to show that no anopheline mosquitoes had been reported between 6th October and 16th November 1946.

The text occupies 14 foolscap pages but there are 40 pages of tables, charts, maps and samples of the forms used as well as 35 photographs. It was read before the Tropical Hygiene Section of the Health Congress of the Royal Sanitary Institute in June 1947.

A careful search of the 1946 eradication area has, up to 10th February 1947, revealed no adults and no larvae of *A. superpictus* a few larvae of *A. claviger* and *A. marleri* have been found in isolated waters.

In this paper, the total cost of the scheme for 1946 is put at £18,000 which represents ten shillings per head of the population or £36 per square mile. In the discussion following the paper it was pointed out that the work in Cyprus emphasized once again the fact that every malaria problem is a local one. This was illustrated by one point, that in the *superpictus* eradication work the fit type of sprayer suited the conditions in Cyprus and was the most economical, isolated patches of water could not be economically dealt with by the drop method as used in the Sudan. The author was unable to give figures for the amount of DDT used per acre, but the amount of larvicide used by one man per

day averaged about one gallon. Wells were treated with the same larvicide as surface water and it was also used to spray the sides of the wells to kill resting adults.

The campaign for 1947 is planned to take in half the island, and in preparation, a winter scheme is in progress consisting of an attack on adult haunts with DDT in gas oil.

H. S. LARSON

PURI, I. M. RAJENDAR PAL KRISHNASWAMI A. K. BHATIA, M. L.  
Studies on some insecticides against Anopheline Adults and Larvae. I. Preliminary Experiments at Delhi with DDT [PURI & RAJENDAR PAL]. *Indian J. Malariology* 1947 Mar v 1 No. 1 133-58, 7 graphs. [16 refs.]. II. DDT as Residual and Space Spray and as Larvicide [PURI & KRISHNASWAMI]. *Ibid* 159-81 28 graphs. III. Experiment with DDT as a Residual Spray in some Villages in Baluchistan [PURI & BHATIA]. *Ibid*. 183-91 3 graphs. IV. Experiments with DDT and 666 as Residual Spray in some Villages around Delhi in 1946 [PURI & KRISHNASWAMI]. *Ibid*. 193-209 7 graphs.

Staff of the Malaria Institute of India have conducted experiments to assess the potentialities of DDT as a mosquitocide and larvicide and to study methods of application under Indian conditions. Their results are largely confirmatory of the work of workers in other countries, but in publishing them they have performed a valuable service for field workers in India.

### *Part I Preliminary Experiments at Delhi with DDT*

The materials used were mainly 5 per cent. DDT solution in kerosene, malanol or used engine oil and DDT turpentine emulsion the method of preparation is fully described. The results were as follows —

Larvicide (a) DDT in oil was very effective in doses of 4 to 6 cc. per 10 sq. yards.

(b) DDT turpentine emulsion is more effective than ( ) thus 2 to 4 cc. of 5 per cent. emulsion (100 to 200 mgm. of DDT) per 10 sq. yds. gave 100 per cent. control for 5 to 8 days and partial control for 12 days.

(c) Aerial spraying is wasteful and very erratic

Residual-Insecticide Both oil and emulsion produced, in mud huts, a 100 per cent. reduction in adult mosquitoes during the first four days, with a partial residual effect persisting for four to five weeks the dose was 150 mgm. to 200 mgm. per sq. foot.

### *Part II*

#### *1 DDT as Larvicide Nilgiris South India*

Tabulated results show the effect of 5 per cent. DDT in a turpentine emulsion and in solution in kerosene, used engine oil and malanol, when applied to flowing streams, to still water in pits and to fallow or growing ricefields. In still water 0.6 cc. of solution per 10 sq. yds. as compared to 3 to 4 cc. in stream or ricefield, was sufficient to produce 100 per cent. kill. A residual effect for 6 to 8 days was evident in ricefields with doses of 2 to 5 cc. of 5 per cent. solution per 10 sq. yards. Higher aquatic fauna appeared to be unaffected.

#### *2 DDT as an indoor residual spray Bengal Town*

Graphs illustrate the effect on indoor anopheline populations of a single application of a 5 per cent. solution or emulsion at a dose of 1 quart per 1,000 sq. ft. of mud plaster surface. Results for solution or emulsion were similar at nearly 100 per cent. reduction for a number of days, the residual

toxicity lasting for two months, increased dosage did not lengthen this period  
*A. minimus* was more sensitive to the residual action than other anophelines

### 3 DDT as an outdoor residual spray Bengal, Terai

Bushes, fences, lanes and the outer surfaces of walls and roofs of huts in a 50-yard belt surrounding groups of dwellings were sprayed with the various 5 per cent DDT solutions or emulsion. Results are depicted graphically and indicate that a dose of 1 to 3 gallons per acre caused an appreciable reduction in the indoor mosquito population for periods up to 13 days. *A. minimus* in particular reappeared later than other mosquitoes. Rainfall vitiated the residual action.

4 DDT as a space spray (5 per cent DDT-kerosene solution) Bengal, Terai  
 This solution used in the interior of dwellings twice a week for three months resulted in a marked reduction of the sporozoite rate among *A. minimus*. As a malaria control measure this is as effective as the use of pyrethrum spray.

### Part III

Quetta (Baluchistan) was selected for further experiments with DDT as a residual indoor spray, because it differed from previous areas of Papers I and II in having a short malaria and mosquito season, and in having *A. superpictus* as the main vector mosquito. A dose of 50 mgm per sq ft reduced the mosquito population to negligible numbers for 10 weeks. A dose of 25 mgm per sq ft though not producing a 100 per cent reduction in numbers of mosquitoes, did appear to reduce the sporozoite rate among *A. superpictus* present.

### Part IV

Experiments were conducted in the Delhi area to compare the efficiency of DDT and Gammexane as residual insecticides. The authors, although making observations on the results with DDT, were not prepared to express an opinion on Gammexane because "the experimental conditions under which this test was carried out" did not permit it.

R Ford Tredre

PURI, I M The Practical Application of DDT for Malaria Control in Rural and Urban Areas in India *Indian J. Malariology* 1947, Mar., v 1, No 1, 211-20

This paper summarizes the previous four and has reference to costs which are of little assistance outside India.

R Ford Tredre

BRESCIA, F & WILSON I B Treatment of Native Villages with the Aerosol Generator *J. Econom. Entom.* 1947, June v 40, No 3, 313-16

[The paper begins with the alarming phrase "Two villages were treated to determine whether an oil-DDT aerosol generated outside native huts can kill adults resting inside the huts during the course of treatment." It seems, however that mosquito adults are implied.]

The villages were thatched native villages in the Solomon Islands. No details of the generator are given, but it is stated that it produces an aerosol with particles of 10-microns diameter. A dosage of 5 lb DDT per 1,000 feet of front was sufficient to destroy *Anopheles farauti* inside and outside the huts and to kill larvae but it only gave a protective period of five days in one village and one day in another. [The front is the distance covered by the generator carrier.] To obtain "an appreciable" protective period it is necessary to use 20 lb of DDT per 1,000 feet of front (the front extending 2,000 ft beyond the

village) if breeding occurs in pools over 1 000 feet from the village. Where breeding is restricted to pools less than 1,000 feet from the village, a dosage of 10 lb. DDT should suffice.

J. R. BARNES

HIDMAM E. H. & CUTKOMP L. K. Block Residual Spraying of Premises with DDT for the Control of Malaria. *Amer J Trop Med.* 1947 July v 17 No. 4 449-61 1 map.

As a result of the experimental work by HINES and KEMMER [this Bulletin 1947 v 44 880] in the Tennessee Valley the DDT residual spray technique has been applied to an area adjacent to the Wheeler Reservoir (Tennessee Valley Authority) in North Alabama (35°N 87°W) a neighbouring area being used for control purposes. The treated district contained 299 occupied premises in 38 sq miles, compared with 238 in 33 sq miles in the untreated control district. Approximately the same percentage of mosquito-proofed residences were present in the two districts.

The interiors of all types of structures (houses barns, privies, animal habitations etc.) were treated with 5 per cent. emulsion of DDT (Stock solution 25 per cent. DDT 73 per cent. Xylene, 2 per cent. Triton) by means of knapsack sprayers rate of application approximated 200 mgm. of DDT per sq. foot costs, excluding supervision, were at the rate of 0.61 dollar per 1 000 sq. feet.

The reduction in numbers of the vector anopheline, *A. quadrimaculatus*, is evident in the following table.

Average number of *A. quadrimaculatus* mosquitoes per premise

Area	Pre-Treatment Inspection	Post Treatment Inspections								
		July			August			September		
	June	1	2	3	4	5	6	7	8	9
Sprayed	20.00	0.4	0.4	0.9	1.1	1.2	1.2	2.1	2.8	6.2
Control	23.3	32.9	32.1	35.6	43.8	31.1	13.1	15.1	29.4	14.2

The figures are based on the total numbers caught in all structures on premise.

Catches of adult mosquitoes in certain unsprayed sections of barns and in well-placed traps, and larval density surveys in adjacent breeding waters, showed that high production of mosquitoes continued despite the premise spraying.

Examination of thick blood films of 90 per cent. of the inhabitants of both districts was completely negative and no conclusion is possible on the effect of the spraying on malaria transmission.

As a result of this experiment and previous information on human blood-feeding of *A. quadrimaculatus* the authors are of opinion that DDT residual spraying of all structures offers more protection against malaria transmission than mosquito-proofing

R. Ford TREBLE

CUTKOMP L. K. Residual Sprays to control *Anopheles quadrimaculatus*. *J Econom. Entom.* 1947 June v 40 No. 3 328-33 3 figs.

The paper reports tests in the laboratory and in unoccupied houses, of various insecticides applied at rates of 100-250 mgm. per sq. ft. The toxicity at different

tunes was judged by the exposure period necessary to cause knockdown of *A. quadrimaculatus*, the experience of the author being that mosquitoes thus affected never recovered (except, sometimes, with pyrethrins)

The results showed pyrethrins and then gamma benzene hexachloride to be most toxic according to this criterion, followed by DDT and "Chlordane" ( $C_{10}H_6Cl_8$ ) and, finally, "Toxaphene" ( $C_{10}H_{10}Cl_8$ ). The residual action of DDT was greatest, followed by those of benzene hexachloride and "Toxaphene", which declined somewhat after fifteen weeks but, under some conditions, were still effective at the end of a year. Pyrethrins and "Chlordane" were least persistent.

An experiment was performed to compare the irritant effects of the various insecticides, calculating the percentages of mosquitoes leaving treated houses in which they were liberated. The figures observed were —

Houses treated with—	(200 mgm /sq ft)	80 per cent left the houses
Pyrethrins	250	57
DDT	100	83
Benzene hexachloride	160	35
Toxaphene		" "

J R Busvine

DAVIDSON, G Field Trials with "Gammexane" as a means of Malaria Control by Adult Mosquito Destruction in Sierra Leone I The Effect of "Gammexane" on Mosquitoes *Ann Trop Med & Parasit* 1947, Sept, v 41, No 2 178-209 2 maps, 2 text figs & 12 figs on 3 pls

The insecticidal properties of hexachlorocyclohexane (benzene hexachloride,  $C_6H_6Cl_6$ ) were first noted in 1942 by Imperial Chemical Industries Ltd, and in 1943 the active insecticidal constituent, the gamma isomer, Gammexane, was isolated.

Various workers showed by laboratory experiment that Gammexane is lethal to mosquitoes in smaller concentrations than DDT, and is quicker in its action. This paper describes experiments conducted in Sierra Leone to measure the value of Gammexane for the destruction of adult *Anopheles gambu*.

Three groups of villages were selected

(a) A coastal group at the foot of the mountains on the open sea

(b) An inland group in the Protectorate associated with mining

(c) A single large village on the Freetown estuary

*Smoke Generators containing Gammexane* A trial of this method in four villages proved it to be inefficient mainly because of the impossibility of sealing the type of house

*Residual Sprays containing Gammexane* Detailed description is given of products used, machines for, and technique of spraying. The walls of houses had a variety of surfaces, wood mud thatch, concrete and corrugated iron.

A detailed analysis of the results in each sprayed village and of the variations of mosquito density in the unsprayed control villages is given. These results may be summarized as follows —

- 1 Gammexane in the form of a residual spray is an efficient means of reducing the population of mosquitoes in houses
- 2 0.5 per cent solution applied at rate of 10 mgm per square foot (4 pints of solution or mixture to 1,000 sq ft) to every available internal wall surface of all houses will reduce the mosquito population in the houses to almost nil for a period of six months
- 3 A lowering of mosquito density in unsprayed houses in adjacent areas was noted

4. In admittedly small numbers of dissections 247 from treated and 159 from untreated villages, the sporozoite rate was 2 per cent. in the former compared to 4.4 per cent. in the latter

R. Ford T. citv

DAVIDSON G. Field Trials with "Gammaxane" as a means of Malaria Control by Adult Mosquito Destruction in Sierra Leone. II. The Effect of Treatment of Houses with "Gammaxane" on the Malaria-Rate in the Inhabitants. *Ann Trop Med & Parasit.* 1947 Sept., v 41 No. 2, 210-14.

By the (owl)-cell technique of Christophers, Sinton and Corvell, malarial parasite count distribution, in addition to parasite rate was estimated from the blood of children in the 0-10 years age-group in selected groups of villages before and five months after spraying with Gammaxane [see preceding abstract]

The results may be summarized as follows —

Locality	No. Examined	Parasite Rate per cent.	Parasite-count distribution (A per cent.)			
			0-500 per cent.	500-1,000 per cent.	1,000-3,000 per cent.	Over 3,000 per cent.
<i>Coastal Villages</i>						
Before treatment	180	81.5	65	9	11	15
After treatment	111	80.2	50	9	20	21
Untreated	68	85.2	40	34	13	13
<i>Interior Villages</i>						
Before treatment	222	85.3	54	17	19	10
After treatment	168	73.6	56	17	16	11
Untreated	51	0.6	91	6	3	0

It is clear that little difference in parasite rates and intensities occurred in the few months of observation.

[These papers do not lend themselves readily to abstraction, and should be studied in the original. Further researches in the field are in progress.]

R. Ford T. citv

RITA, G. & GRAMICIA, G. Ricerche sulla infezione degli embrioni di pollo con *Plasmodium gallinaceum* (I nota) [Infection of Chick Embryos with *P. gallinaceum*] *Riv di Parasit.* Roma. 1947 June-Sept., v 8 Nos. 23, 119-24 2 figs. [12 refs.] English summary (6 lines)

The authors attempted to inoculate 25 embryo chicks from the 9th to the 17th day of incubation. Heavily infected blood was applied to the chorio-allantoic membrane and a small quantity was injected into the vitelline sac. Only two of the chickens, both of the 9th day acquired an infection. The infection developed rapidly death occurring on the 5th day after hatching. The parasites, which revealed an abnormal morphology were readily inoculable to other chickens the parasites then regaining their normal appearance.

C. M. Wray

KROPPERS, A. T. Acquired Resistance (Twofold) to Quinine in *Plasmodium gallinaceum*. [Correspondence.] *Nature*. 1947 Nov 1 608-7

It was recently shown by BISHOP & BIRKETT and by WILLIAMSON & AL. [the *Bulletin* 1947 v 44 969-970] that *P. gallinaceum* maintained in chickens



could acquire resistance to paludrine. The present author has obtained similar results, but in contrast to the findings of the latter authors an acquired resistance was also demonstrated in the case of quinine. This result was obtained by inoculation of a 7-day-old chick with 50 million parasites followed by treatment with the minimal effective dose of the drug given once on the day of inoculation and twice on each of the three following days. Reinoculation of a fresh host was carried out with the blood of a treated animal on the same day each week. After treatment of the chickens with 10 mgm /kgm of quinine base in the form of hydrochloride, as in the above dosage schedule, some resistance was apparent after 12 weeks. After a further 16 weeks' treatment with double the dose, the course of the infection was scarcely influenced. The degree of resistance was found by experiment to be twofold. After one passage of the resistant strain through *Aedes aegypti* this acquired resistance to quinine was partially lost. The quinine-resistant strain showed no such character towards mepacrine paludrine, or chloroquine.

J D Fulton

RAGER, W. The Relation to the Course of Avian Malaria of Biotin and a Fat-Soluble Material having the Biological Activities of Biotin. *J Exper Med* 1947, June 1, v 85 No 6, 663-83, 6 figs [36 refs]

In a previous paper [this *Bulletin*, 1943 v 40, 825] the author produced evidence that deficiency of biotin lessened the resistance of chickens and ducks to malaria infections. He subsequently found [*Proc Soc Exper Biol & Med*, 1947, v 64, 129] that the plasma of various animal species after hydrolysis with acids or enzymes contains a fat-soluble material designated FSF, having the biological activity of biotin, but differing from it chemically and which is not inactivated by the avidin of egg white. This substance could replace biotin as a growth factor for *Lactobacillus casei*. Its biotin activity has been used to measure the concentration of the substance, possibly a lipoprotein, from which it arises. Its properties suggest that it is concerned with resistance to infection. Chicks infected with *P. lophurae* and ducks infected with the same parasite or *P. cathemerium* were used in these experiments. The various diets used, which were adequate or deficient in biotin, are described. During malaria infections, the changes in concentration of biotin and of FSF in plasma and organs were measured by a biological method with the use of *L. casei*. Free biotin and FSF were measured in untreated plasma. The difference between that value and the one obtained after hydrolysis gave the value for bound FSF, biotin itself being unbound. The early inhibition of multiplication of *P. cathemerium* in ducks moderately deficient in biotin was paralleled by the deficiency of riboflavin and pantothenate in other malaria infections of chickens and by vitamin C deficiencies in monkeys, being due probably to the absence of a specific growth factor for the parasites. The higher peak of infection finally reached in deficient hosts suggested that another factor was at work, which interfered with some defence mechanism of the hosts, other than leucocytes. The concentration of bound FSF in plasma during infection varied to some extent like that of biotin, but the return to normal levels was longer delayed. Whereas the presence of excess free biotin is not associated with a limitation of parasite multiplication, high levels of bound FSF appeared to be associated with increased resistance to parasite growth. After malaria infections, the biotin content of the livers of deficient animals was reduced. In experiments with *P. lophurae in vitro*, in which the biotin content of the medium varied widely, the rate of parasite multiplication was not affected. The addition of  $\alpha$  and  $\beta$  globulin fractions from human plasma having a 2 per cent concentration of FSF caused haemolysis and degeneration of the parasites. Similar effects have been noted with

fractions of animal plasma. The results support the view that the PSF fraction arises from a substance, probably a lipoprotein which is associated with resistance to malarial avian infection and acts against parasites and sensitized erythrocytes.

J D Fulton

## BLACKWATER FEVER

KOLFF W J with the cooperation of J VAN NOORDWIJK. *The Artificial Kidney* 92 pp. 46 figs. 4 plans (1 folding) 1 chart & 5 sketches. [21 refs.]. 1946. Kampen, Holland J H. Rok NV.

It is not improbable that the accumulation of diffusible metabolic products in the blood is a contributory cause of death in acute uraemia. The removal of such retention products from the blood stream during the period of acute renal failure might help to keep the patient alive until such time as normal renal function is re-established. This book describes in considerable detail a method of removing such products from the blood by dialysis, by the use of a machine which the author has called "the artificial kidney". Other methods, such as irrigation of the peritoneal cavity and perfusion of isolated loops of gut, have occasionally been tried with some success. Kolff's method is based on extra-corporeal dialysis of the patient's blood by a method rather similar to that previously described by Abel and his colleagues [ABEL, ROWNTREE & TURNER, *J Pharmacol.* 1913 v 5 275]. The machine consists of a cellophane tube 30-45 metres long wrapped round a rotating cylinder a portion of which is immersed in rinsing fluid which is a solution of sodium chloride (0.6 per cent.) sodium bicarbonate (0.2 per cent.) potassium chloride (0.04 per cent.) and glucose (1.5-2.0 per cent.). Arterial blood from the patient is passed into the cellophane tube and returned, after dialysis, by means of a cannula inserted into the patient's vein. The artificial kidney can deal with up to half a litre of blood at any one time and large quantities of blood can be dialysed in it in a short period. Thus in one case 80 litres of blood passed through it in under 12 hours. Kolff has reported the use of his artificial kidney in 17 cases of chronic and acute uraemia. In this series there were 2 recoveries. He has since reported 8 additional cases with 3 more recoveries [*Lancet*, 1946 Nov 16 726]. Extra-corporeal dialysis of blood in large volumes appears now to be a practicable proposition provided the apparatus is to hand. As was pointed out in the leading article in the *Lancet* [1946, Nov 16, 720] Dr Kolff "has provided evidence indicating that in some cases dialysis may tide the patient over a period of acute renal failure and keep him going until renal function is restored. The technique should be of value in those cases of potentially reversible renal failure which have been called renal anoxia [MARGRAITH HAVARD & PARSONS (this *Bulletin* 1945 v 42, 968)] in Britain and lower nephron nephrosis" in America, [LOCKE *Milit. Surgeon* 1946 v 99 371]. It is hoped that one day the opportunity may arise to test this technique in anuric blackwater fever.

B G Margraith

GOODYEAR, W E. & BEARD D E. *The Successful Treatment of Acute Renal Failure by Peritoneal Irrigation.* *J Amer Med. Ass.* 1947 Apr 19 v 133 No. 16, 1208-10 2 figs.

The possibility that death, in acute renal failure of a reversible kind, may be due to the accumulation of substances normally excreted by the kidneys, has given rise to the development of several methods of removing such substances from the blood, and so prolonging life until the kidneys can recover sufficiently

to resume function One of the techniques which has lately been stressed is based on a method of dialysis of the patient's blood by a machine which has been called the artificial kidney by its designers (KOLFF and BERK, *Acta Med Scandinavica*, 1944, v 117, 121), [see also above] This consists of a "cellophane" tube partly immersed in a solution of sodium chloride, sodium bicarbonate, potassium chloride and glucose Blood from the patient is passed through this apparatus from a cannula in the radial artery, and back into the body by a cannula into a vein of the foot or forearm In this way, substances such as excess urea are dialysed

The present authors have used an alternative method and have utilized the NaCl 8.0 gm KCl 0.2 gm,  $\text{CaCl}_2$  0.1 gm,  $\text{MgCl}_2$  0.1 gm,  $\text{NaHCO}_3$  1.0 gm, peritoneum as the dialysing area The irrigating fluid contained (per litre), sodium biphosphate 0.05 gm, dextrose 1.5 gm, heparin 0.5 mgm, penicillin 5,000 units, and sulphadiazine sodium 0.1 gm Catheters were inserted into the peritoneal space and the incision was closed The irrigating solution was admitted to the peritoneal cavity by a drip method The average rate of irrigation was 500 cc per hour for two days, and 300 cc per hour for the two following days The technique was tried in a white woman who developed a reaction subsequent to transfusion following a nephrectomy The reaction was complicated by suppression of urine and rapidly increasing azotaemia Peritoneal irrigation was instituted 84 hours after the nephrectomy, and continuous irrigation was maintained for 4 days The azotaemia was rapidly reduced and the urinary output rose from 20 cc to 240 cc per day There was remarkable clinical improvement The non-protein nitrogen of the blood reached 100 mgm per cent within 3 days of the discontinuation of the peritoneal irrigation, but the urinary output steadily rose and the patient made an uninterrupted recovery The urea content of the recovered peritoneal washings varied from 47 to 53 mgm per cent The urine excreted after a resumption of renal function had a urea content of 100-140 mgm per cent and a specific gravity of 1.010-1.012 [The interest of this case from the point of view of tropical medicine lies in the possible application of such methods to cases of renal failure of the renal anoxic type occurring, for example, in blackwater fever or cholera It is possible that an artificial kidney of the type described by Kolff and Berk might give more satisfactory results as far as dialysis of the blood is concerned] [A case of peritoneal irrigation for uraemia after an incompatible blood transfusion is described by MUIRHEAD *et al* (*Arch. Surgery*, 1947 v 54, 374) Ed]

B G Maegraith

## TRYPANOSOMIASIS

NIGERIA Sleeping Sickness Service Annual Report 1946 *Nigeria Rep. on Med Services for Year 1946* 22-9 1947 London 4 Millbank, SW 1 [9d]

Abstracted from a mimeographed copy, in this *Bulletin* 1947 v 44 973 5

NODENOT, L Note sur le traitement de la maladie du sommeil par la pentamidine [The Treatment of Sleeping Sickness with Pentamidine] *Bull Méd de l'Afrique Occidentale Française* 1946, v 3, No 2 215-26 [23 refs]

Results obtained with pentamidine [presumably the isethionate], in the treatment of sleeping sickness at Bobo-Dioulasso since 1944 may be summarized in the table below, constructed from the author's text

*First series. Followed for 6 to 10 months some for more than 1 year*

Type of case		Pentamidine treatment, i.m. repeated for 6 doses*	Cases	Possibly cured	No improvement†	Relapsed
Early	Previously untreated	2 mgm./kgm.	78	73	2	1
		3 "	4	4		
	Reinfection	2 "	2	2		
	Arseno-resistant relapse	2 "	3	3		
		3	1	1		
Late	Previously untreated	2 followed by trypanamide‡	10	5	5	
	Chemo-resistant§		9	2	7 (6)	

*Second series. Followed for shorter periods than the first series.*

Early	Previously untreated	4 mgm./kgm.	60	56	4	
Late	Slightly altered c.s.f.	4	10	4	6	
		4 ††	3	2	1	
		6	7	4	3	
		6 ††	2	2		
	Much altered c.s.f.	4-6 plus intrathecal treatment‡§	14	0	14 (6)	
	Chemo-resistant§	4 mgm./kgm.	20	4	16 (2)	
		Lm. plus intrathecal treatment‡§	21	0	21 (9)	

\*On alternate days for 1st series daily for 2nd series.

†Number of deaths shown in brackets.

‡Course of 10 intravenous injections.

§Previously unimproved by treatment with arsenicals and suramin.

\*\*Details of c.s.f. changes not stated.

††Re-treatment of uncured patients of group immediately above. Treated 1 month after end of previous course.

‡Using 1 per cent. pentamidine, further diluted in c.s.f. in the syringe before injecting. First cases treated with 3 doses of 16 mgm. given after 1st, 3rd and 5th i.m. injections. Later cases treated with 1 or 2 doses of 10 mgm.

The author concludes that a dose of 2 mgm./kgm. pentamidine per injection is hardly sufficient, and 3 mgm./kgm. is recommended. In high dosage the

drug is effective up to, but no later than, the time when the infection begins to involve the central nervous system  
 Intrathecal treatment is extremely toxic, and generally aggravates the infection  
 See also p 201 WOODMAN, Nutrition of the African in Tsetse-Fly Areas.  
 E M Lourie

MAZZOTTI, L Presencia en Mexico de *Triatoma protracta* woodi Usinger y de *Triatoma gerstaeckeri* (Stål) [Presence in Mexico of *Triatoma protracta* woodi Usinger and *Triatoma gerstaeckeri* (Stål)] *Rev Inst Salubridad y Enfermedades Trop* Mexico 1947 Mar, v 8, No 1 69-70

This paper records the finding of *Triatoma protracta* woodi in the State of Coahuila, Mexico In the same area, specimens of *T. gerstaeckeri* were collected this species has previously been recorded in the State of Nuevo León in 19 Both species were found to be infected naturally with *Trypanosoma cruzi* The insects were found in nests of *Neotoma micropus canescens*, on which they appear to feed  
 H J O'D Burke-Gaffney

## LEISHMANIASIS

LUENGO ARROYO E NÁJERA ANGULO, L & LOZANO MORALES A Problema sanitario de la leishmaniasis visceral mediterranea en España (Ponencia oficial) [The Problem of Visceral Leishmaniasis in Spain from the Sanitation Aspect] *Kuba Habana* 1947, Aug, v 3, No 8, 167-77, 1 fig

Since the report of PITTALUGA and VILÁ of the finding of cases of infantile kala azar in Spain in 1912 some 2 000 cases have been recorded In the year ending 31st May, 1946, there were 138 noted in 13 Provinces, the most, 31, in Jaén, next, 28, in Toledo, fewest, one only, in Madrid  
 The authors consider the question of geographical distribution (just related) the aetiology, diagnosis and treatment, the epidemiology and prevention  
 Diagnosis was made on clinical, haematological and serological grounds, such as the globulin tests of Brahmachari, the ureastibamine test of Chopra and Das Gupta, the antimony-formol test of Nattan-Larrier, the sulpharsenol test of Caminopetros, and others, or by the intradermo-reaction or by deviation of complement, by spleen or marrow puncture The authors have nothing fresh to add on the subject of treatment As regards epidemiology they suggest that besides the dog, the squirrel *Xerus getulus*, may be a reservoir host  
 H Harold Scott

KIRK R & LEWIS, D J Studies in Leishmaniasis in the Anglo-Egyptian Sudan IX Further Observations on the Sandflies (*Phlebotomus*) of the Sudan *Trans Roy Soc Trop Med & Hyg* 1947, July, v 40, No 6, 869-88 2 maps & 2 figs [44 refs]

The collecting of sandflies in the Sudan by the oiled-paper method has resulted in the finding of 25 species of *Phlebotomus* these are listed and the bionomics of some are described  
*P. langeroni* var *orientalis* is the only one of the *P. major* group whose distribution is related to that of kala azar in the Sudan Its occurrence is erratic and variable and may have some bearing on the erratic and variable

occurrence of kala azar. Unpublished observations revealed the anterior development of the parasites in gorged females which had fed on a patient with post-kala azar dermal leishmaniasis.

The common outdoor species *P. chylsi* bites man in and out of doors. In experiments, the development of flagellates has been observed in one out of forty specimens, but the development was not of the "anterior" type.

The commonest and most widely distributed species is *P. signatipennis* but it feeds on geckos and seldom or never on man.

*P. papatasi* readily bites man indoors and has also been observed to bite outside.

The authors have made a special study of the haunts of *Phlebotomus* adults, particularly of holes and cracks in the ground. From observations and trapping experiments, they have accumulated considerable evidence that a vast subterranean environment exists in the Sudan plains, consisting of animal burrows in the sandy parts and of cracks in the heavy clay known as "black cotton soil". These are adult resting places, but whether they are also breeding places is not certain as no thorough search was made for immature stages.

H S Lacey

ANSARI, N. *Leishmaniose experimentale à L. tropica chez la souris*. [Experimental Leishmaniasis produced in the Mouse by *L. tropica*.] *Bull. Soc. Path. Exot.* 1947 v 40 Nos. 3/4 82-6 4 figs. on 2 pls.

Using a strain of *L. tropica* isolated in culture (N.N.N. medium) from facial lesions of a girl suffering from Oriental sore the author inoculated 108 young white mice by intradermal, intratesticular and intraperitoneal routes. Intradermal injection at the base of the tail produced in 4 out of 8 mice cutaneous lesions at the site of inoculation in one case accompanied by visceral infection. Intraperitoneal injection of 22 mice resulted in a generalized infection varying in severity in 17 cases. The most constant positive results were obtained after intratesticular inoculation of 78 mice, 67 of which acquired a generalized infection while in 6 cases the infection was restricted to the testes. In each of the above series, a number of mice were refractory. The incubation period of experimental leishmaniasis in mice varied from 60 to 90 days. As a rule the mice succumbed to the infection in from 88 to 188 days. The occurrence of parasites, as revealed in smears, varied in different organs and tissues which are arranged in the descending order of frequency as follows: testes, ganglia, spleen, liver, peritoneum, bone-marrow, kidneys, lungs and suprarenal glands. The histo-pathological findings which are described in detail, can be summarized as follows. At the point of inoculation there appears a granuloma consisting mainly of macrophages loaded with leishmanias. The granuloma undergoes secondary necrosis and gives rise to a lesion closely resembling that of oriental sore in man. This localized lesion is followed by a generalization of the pathological process, which spreads to the spleen, ganglia, bone-marrow, liver and lungs involving the reticulo-endothelial system exclusively: the cells of which are packed with parasites. This process of infiltration representing a veritable parasitic blockade is accompanied by proliferation of cells of the reticulo-endothelial system which is especially marked in the spleen and liver giving rise to histo-pathological changes resembling those in kala azar. [The paper is illustrated by 3 photographs and one photomicrograph.] C A Howe

SEAGER, L. D. & CASTELNUOVO GINA. Toxicity of Stilbamidine. "A Study of the Effects of Chronic Intoxication." *Arch. Pathology*, 1947 Sept., v 44 No. 3 287-96, 4 figs. [Refs. in footnotes.]

The toxic effects of stilbamidine on animals have been reported by number of workers [this *Bulletin* 1940 v 37 700 1943 v 40 663 1945 v 42, 18

1946, v 43, 1029] The present authors have investigated the histological changes produced by this substance after different dosage schedules in 160 rabbits and 100 mice. Many organs and tissues were studied, but the changes, chiefly degenerative, were most marked in liver and kidney. Detailed descriptions are recorded for these organs in animals killed at various intervals after drug administration. The nervous system was not investigated. Rabbits were treated subcutaneously with the drug and mice by the same route as well as by stomach tube. The doses ranged from 10 to 100 mgm per kilo and were given in single or multiple injections. During treatment rabbits lost weight, had diarrhoea and suffered from weakness, congestion of the iris and fall in blood pressure. Attempts to counteract these conditions were not successful. Blood sugar estimations indicated a hyper- or hypoglycaemic condition at different times, those for blood urea nitrogen were inconclusive while the van den Bergh test became positive after a short time. The chief change in the blood picture was a shift to the left in the leucocyte count, nucleated red cells were sometimes seen. Mice proved more tolerant of the drug, but changes comparable with those seen in the rabbit tissues were noted. There appeared to be no correlation between dosage and the histological picture.

J D Fulton

### FEVERS OF THE TYPHUS GROUP

BUSTAMANTE, M E & VARELA, G. Distribución de las rickettsiasis en Mexico (Tifo murino, tifo clasico y fiebre manchada) [Distribution of Rickettsial Disease in Mexico (Murine and Epidemic Typhus and Rocky Mountain Spotted Fever)] *Rev Inst Salubridad y Enfermedades Trop Mexico* 1947 Mar, v 8, No 1, 3-14, 5 maps & 3 figs [17 refs] English summary

The incidence in Mexican States of the three rickettsial diseases in question is discussed and shown in a table. In each case the presence of the disease was established by the isolation of strains or by complement fixation or both. Murine typhus was found in 18 States and epidemic typhus in 19 which included 12 which also had the murine type. In the States of Durango and Sinaloa murine typhus and Rocky Mountain spotted fever were both present, in Coahuila all three rickettsial diseases were found, in San Luis Potosi and Vera Cruz both epidemic typhus and spotted fever were identified and the latter was also isolated in Sonora. The distribution of the three diseases singly and together, are shown in 4 maps, and the mortality from typhus in Mexico between 1931 and 1942 is shown in another map. In the north and north-east regions of Mexico, *Rhipicephalus sanguineus* was found naturally infected with the virus of Rocky Mountain spotted fever, on the east coast, the vector was *Amblyomma cajennense*.

RAYNAL, J H. La rencontre des *Proteus* à l'occasion du typhus de Chang-Hai [The Incidence of *Proteus* Strains during the Epidemic of Typhus Fever at Shanghai] *Bull Soc Path Exot* 1947, v 40, Nos 7/8 294-304, 1 chart [11 refs]

H J O'D Burke-Gaffney

No strains of *Proteus* were isolated from any of the 300 blood cultures made between 1938 and 1945 in Shanghai during the early stages of attacks of fever which were afterwards found to be due to typhus infection. From animals experimentally infected with typhus rickettsiae large numbers of heart-blood cultures were made after death, *Proteus* organisms were isolated

from 10 per cent. of the white mice examined, from 1.7 per cent. of the white rats, and from only one of several hundreds of the guinea-pigs.

From wild rats, about 3 000 blood cultures were made—only eight strains of *Proteus* were isolated, but 71 strains were isolated from bone-marrow cultures and 148 from urine cultures.

Among the 301 strains isolated in all the above experiments, 17 behaved like *Proteus OX19* in agglutination tests—eight like *P. OXX* and one like *P. OXE*. An unstated number reacted in a manner suggesting that they belonged to types intermediate between *Proteus vulgaris* and *Proteus X*.

John W. D. Meigs

DE ROSNAY D. Etude de la moelle osseuse dans le typhus exanthématique. [The Bone Marrow in Epidemic Typhus.] *J. Méd. de Bordeaux*, 1947 Oct. v 124 No 10 480.

In 48 cases of epidemic typhus, the author studied specimens of bone marrow obtained by sternal puncture. He states that the myelogram obtained is characterized by changes in the red cell and myeloid systems and particularly by a definite proliferation of reticulo-endothelial and other elements. These changes are early and, the author states, give the myelogram a very characteristic appearance. Nevertheless, he admits that the changes are not specific but they do indicate a reticulo-endothelial response of an intensity rarely encountered in other infections—hence he considers that they have some diagnostic value in difficult cases.

By means of special staining techniques such as hot Giemsa or Gioud's application of Macchiavello's method, cellular inclusions may be seen in some reticulo-endothelial cells in marrow smears—these inclusions recall the forms described by GIROUD and PANTHEIS (this *Bulletin* 1942, v 39 753) in the lungs of animals inoculated intratracheally with rickettsiae, and named by them homogeneous bodies.

The author is not prepared, however, on a simple morphological similarity alone to assign a rickettsial nature to the inclusions seen in the bone marrow in epidemic typhus. Nevertheless, as these appearances are not seen in normal marrow nor in persons suffering from other infections, they have a considerable diagnostic value in the haematological study of epidemic typhus.

H. J. O'D. Burke-Gaffney

SANDOR, G. & GIROUD, P. Nature de l'agglutinine anti-typhus du sérum de lapin. [The Nature of the Anti-Typhus Agglutinins of Rabbit Serum.] *C. R. Acad. Sci.* 1947 Oct. 20 v 225 No. 16 704-5

The authors have studied the distribution of the anti-typhus agglutinins in the protein fractions of the serum of rabbits inoculated through the respiratory route with typhus rickettsiae.

Three different euglobulin fractions were isolated from the rabbit serum whereas only two could be isolated from human and equine sera.

One of the euglobulin fractions from each of the above three sera was found to contain the greater part of the anti-typhus agglutinins, but this fraction in the case of the rabbit was not the same as in the case of man or the horse.

For the technical methods employed the original paper must be consulted.

John W. D. Meigs

SUTORISOVA-STULBOVA, Marguerite. Action sensibilisatrice de l'alexine au cours de l'agglutination des rickettsies. [The Sensitizing Action of Complement in connection with the Rickettsia-Agglutination Reaction.] *C. R. Soc. Biol.* 1947 July v 141 Nos. 13/14 719-20

The sensitivity of a formal-killed rickettsial suspension used in carrying out the rickettsia-agglutination test was found to be increased two to eight times



by the addition of complement [In one of the seven tests of which details are given, the rise in the titre was only from 1-40 +++ to 1-40 +++++]

John W D Megaw

GIROUD, P & JUDE, A Conservation du pouvoir agglutinant vis-à-vis des rickettsies des sérums typhiques saturés par le *Proteus OX19* [Retention of the Rickettsia-Agglutination Potency of Typhus Serum after Absorption with *Proteus OX19*] *C R Soc Biol* 1947, July, v 141, Nos 13/14, 721-2

Agglutination tests were carried out on epidemic-typhus serum and on the same serum after absorption with a suspension of a culture of *Proteus OX19* which had been heated to 100°C for 60 minutes. The untreated serum agglutinated *P OX19* at a titre of 1-1,280, whereas after absorption the titre was only 1-80.

In rickettsiae-agglutination tests in which *Rickettsia prowazeki* and *R mooseri* were employed, the titres with untreated serum were 1-1,600 for both organisms, with the absorbed serum, they were 1-3,200 and 1-6,400 respectively.

Three samples of murine-typhus serum were tested in the same way, and with similar results, the absorption of the *OX19* agglutinins tended to increase rather than diminish the rickettsial agglutinins, so it was concluded that specific differences existed between the *Proteus* and rickettsial agglutinins.

John W D Megaw

HORTOPANU, D Gangrenele tifosului exantematic [The Forms of Gangrene in Exanthematic Typhus] *Rev Stiintelor Med* Bucharest 1947, Jan-Apr, v 36, Nos 1/4, 114-24 French summary

The author, in Rumania, reports on the presence of gangrene encountered on 25 occasions among 465 cases of exanthematic typhus seen since 1941. He divides these varieties of gangrene into the following three groups, which he regards as being quite distinct, aetiologically, clinically and therapeutically.

1 *Gangrene from thrombo-arteritis obliterans* of the large arterial vessels is seen especially in the legs. It is unilateral and results in necrosis involving almost the whole limb, but it is fortunately rare, and only 2 cases were seen, in persons of 2½ and 19 years respectively.

This condition begins abruptly with violent pain in the affected limb. After 5 to 6 days of ischaemia, signs of dry gangrene appear. The affected part necroses and is completely mummified in 20 to 30 days. The slough separates in a strikingly clear-cut manner from the healthy living tissues, and this contrast is much more marked than in any other form of gangrene. By the time this has occurred, amputation is confined almost to the dividing of bone, which appears stripped of tissue. Perifemoral sympathectomy or section of the lumbar sympathetic (Leriche's method) should be tried, but are only successful in the first 6 to 8 hours. Acetylcholine should be given at the beginning of the ischaemia, although its effects are rarely marked.

2 *Gangrene limited to the extremities* is distinguished from the preceding variety by its causative lesions, which are the ordinary affections of arterioles as seen in exanthematic typhus. These are seen only in the winter in patients suffering from cold and malnutrition. Unlike (1) above, this form of gangrene begins insidiously and is limited entirely to the extremities, usually the toes. It is bilateral, and sometimes symmetrical. Necrosis is always superficial. Treatment is wholly conservative and surgical intervention is contraindicated in this form.

3 *Thrombo-angitis obliterans* (Bürger) is regarded by the author as a late complication of typhus, which should be taken into account in making a prognosis.

H J O D Burke-Gaffney

SMADIEL, J. E. SMYDER, J. C. JACKSON Elizabeth B., FOX, J. P. & HAMILTON H. L. Chemotherapeutic Effect of Acridine Compounds in Experimental Rickettsial Infections in Embryonated Eggs. *J. Immunology* 1947 Oct., v 57 No 2, 135-71 4 figs. [32 refs.]

During the war reports were received that Fumagander in Germany had found certain acridine drugs effective in preventing the death of mice experimentally infected with murine typhus. The chief substances tested by the authors were nitroacridin 3582 and an arsenical salt of this, called rutenol [see this *Bulletin* 1947 v 44 1037]. The tests were carried out on groups of embryo chicks infected with one of the following strains of rickettsiae *Rickettsia prowazekii*, *R. mooseri*, *R. orientalis* and *Dermacentor* [Rickettsia] *rickettsii*. Both of the substances, when injected in suitable doses into the yolk sacs of embryos inoculated with rickettsiae, produced a definite rickettsiostatic effect and a pronounced delay in the death of the embryo.

Unfortunately the ratio between the therapeutic and toxic doses of the drugs was low 1-2 to 1-4 whereas for para-aminobenzoic acid it was about 1 10. The paper which contains details of a large number of experiments, will be read by all workers on the chemotherapy of the typhus fevers. A useful bibliography with references to 32 articles is appended.

John W. D. Meager

RAVENHILL, S. F. The Treatment of Rocky Mountain Spotted Fever with Para-Aminobenzoic Acid: a Comprehensive Plan. *Southern Med. J.* 1947 Oct. v 40 No. 10 801 11 7 charts. [15 refs.]

A detailed description is given of six cases of Rocky Mountain spotted fever in which para-aminobenzoic acid (PABA) was given with strikingly good results.

The total daily dosage recommended by the author is 0.5 gm. per pound of body weight for large children this amount is given in divided doses every two hours 1.0 gm. per pound is needed for very small children. Every dose is buffered with 10 cc. of a 5.0 per cent. solution of sodium bicarbonate for each gramme of the drug. In exceptional cases the patient refuses to swallow the medicine and gavage is needed. The treatment is kept up till three or four days after the fall of the temperature.

The blood level of the drug should be estimated daily at exactly the same time in relation to the administration of the previous dose. It should be maintained at between 30 and 60 mgm. per 100 cc. levels above 80 mgm. are risky.

If the total white-cell count falls below 3 000 per cmm. the drug should be stopped. Abdominal distension and delirium are not infrequently caused, but they are rarely of serious importance.

Details are given of the general treatment which includes —(1) the preliminary restoration of the fluid and electrolytic balance by glucose in saline given intravenously (2) maintenance of this balance by fluids with added sodium chloride by the mouth (3) correction of acidosis when necessary by parenteral injections of sodium lactate and (4) a diet containing abundant proteins and vitamins.

John W. D. Meager

CAUGHEY, J. E. & DUDGON, J. A. "Q" Fever. A Serological Investigation of a Group of Cases previously reported as Primary Atypical Pneumonia. *Brit. Med. J.* 1947 Nov 1 684-5.

An outbreak in which 511 cases of "primary atypical pneumonia" occurred between February and April, 1945 among British and New Zealand troops in

the Naples-Caserta area was described by ADAMS *et al* [*Bulletin of Hygiene*, 1946, v 21, 288]. Nearly two years later, sera were obtained from 20 of the 50 persons whose attacks had been specially studied. Nineteen of the 20 sera gave positive reactions to the complement-fixation test for Q fever at significant titres ranging from 1-4 to 1-128. The tests were carried out by Dr N H Topping of the National Institute of Health, Bethesda, U S A, the antigen used was an Italian strain of *Rickettsia burneti*.

The outbreak, therefore, appears to have been one of Q fever, of which several outbreaks occurring later in the Mediterranean area were closely studied by American workers, and were identified by the isolation of *R. burneti* and by other tests. Abstracts of 11 papers in which these investigations are described will be found in this *Bulletin*, 1947, v 44, 62-71.

The paper contains a succinct account of the incidence, clinical features, and epidemiology of Q fever in the Mediterranean area, where the disease—though not fatal—caused great concern to the allied medical staffs because of the occurrence of numerous outbreaks in 1944 and 1945.

[Since this abstract was written there has come to hand the September 1947 number of the *Archives of Internal Medicine*, which contains (p 413) a letter from GROSSMAN, referring to a paper by him in those *Archives* [see *Bulletin of Hygiene*, 1946, v 21, 572]. This paper was an article "purporting to describe an outbreak of primary atypical pneumonia observed in Italy in 1944". On comparing his cases with those of ROBBINS and RAGAN and FEINSTEIN *et al* [this *Bulletin*, 1947, v 44, 62, 66], Dr Grossman now believes that his cases also were those of Q fever.]

John W D Megaw

COMBIESCO D, VASILIU, V & DUMITRESCO, N. Identification d'une nouvelle rickettsiose chez l'homme en Roumanie [Identification of a New Rickettsial Disease in Man in Rumania] *C R Soc Biol* 1947, July, v 141, Nos 13/14, 716-17.

In the late winter and early spring of 1947, the author observed several patients whose symptoms suggested that they were suffering from a "new disease". From the blood of five of the patients, two strains of rickettsiae were isolated by passage, first through guineapigs, and then through chick embryos. Suspensions of blood and organs of the infected guineapigs were still infective after filtration [no details are given of the candles used].

The symptoms were similar to those observed in the various outbreaks of Q fever mentioned in the above abstract, so the authors conclude that the disease was analogous to, if not identical with, Q fever or "Balkan grippe".

John W D Megaw

## BARTONELLOSIS

RICKETTS W L. Carrion's Disease. A Study of the Incubation Period in Thirteen Cases. *Amer J Trop Med* 1947 Sept v 27, No 5, 657-9.

Much controversy has arisen in the past regarding the incubation period of Carrion's disease, which has been variously estimated as being from a few days to several months. Most of these early studies were made in the absence of cultures for *Bartonella bacilliformis*.

The author studied 13 cases of the disease in different hospitals in Lima, Peru, between 1938 and 1942. In all *Bartonella* was demonstrated in the blood, either by culture or direct smear.

All the patients had been healthy before becoming exposed to *Phlebotomus* in the endemic area. There were two groups. In one, there were seven persons

who had only been in endemic zones for a few hours to three days this incubation period was thus accurately estimated. It varied from 20 to 23 days in four cases, and in the other three it was 40, 88 to 90 and 100 respectively. Details are given of two such cases.

In the second group of six persons the incubation period could only be estimated approximately as the persons remained permanently in the endemic area. In these, the period of incubation varied from 19 to 30 days, indicating that infection occurred during first exposure.

The author discusses the former difficulty in establishing the incubation period of Carrion's disease which is attributable mainly to the limited number of observations, the lack of reliability of patients' histories, and the varying symptomatology of the disease.

The vague symptoms met with in the initial stage of atypical and subclinical cases are often interpreted by patients as flu and gastro-intestinal upsets. In the present series, the finding of *Bartonella bacilliformis* in blood cultures taken during these apparently non-specific episodes made diagnosis possible. In Oroya fever the marked anaemia and slight jaundice, with *Bartonella* in the peripheral red blood cells, permit of an early diagnosis.

The author points out that the above findings agree with the result of experimental human inoculations. The first made by Carrion himself indicated an incubation period of 21 days. In the second, KUCZEMSKI-GONZALEZ observed initial symptoms 17 days after he had inoculated himself.

H. J. O. D. Burks-Gaffney

POCKRAT C. M., FRIEDEN E. H. & YEAGER, ENRI. *Bartonella-Endothelial Immune Serum (Bels) V. An Experimental Anemia in Bartonella Infected Rats produced by Anti-Blood Immune Serum.* *J. Infect. Dis.* 1947 Mar-Apr., v. 80 No. 3, 154-63, 4 figs. [20 refs.]

## DENGUE AND ALLIED FEVERS

PAVLOVSKY E. N. *Dengue Fever and Its Vector.* State Medical Publication. 90 pp. 35 text figs. 1947 Leningrad. [In Russian.] [3.75 Roubles.]

The aim of this book is to provide Russian medical officers with a guide to sandfly fever which in the Soviet Union is endemic in the Crimea, in Southern Ukraine, Transcaucasia and Middle Asia. A historical introduction, dealing with the achievements of Russian workers in the study of the disease during the last 25 years, is followed by a chapter in which sandfly fever is defined and data are given regarding its geographical distribution, aetiology, course of infection, diagnosis and treatment. Short chapters are devoted to the properties of the virus and to questions regarding susceptibility of lower animals to the infection. The greater part of the book is concerned with various aspects of the epidemiology of the disease, particular attention being devoted to the vector *Phlebotomus papatasi*, the development and bionomics of which are described in some detail. These data are used as a basis for sandfly control, including methods of protection and destruction employed against these insects, which are fully described. The systematic application of these measures for the prophylaxis of sandfly fever has already resulted in a marked diminution of the incidence of infection in Sebastopol. A separate chapter deals with immunity in sandfly fever.

This book, which provides in concise form all the essential information regarding sandfly fever, is a useful addition to the literature on tropical and subtropical diseases.

C. A. Hoers

## PLAGUE

PUBLIC HEALTH REP Wash 1947, Sept 12, v 62, No 37, 1336-40 **Plague Infection reported in the United States in 1946**

No human case of plague was reported in the United States in 1946, nor has one been notified since 1943 (except for a laboratory infection in San Francisco in 1944)

During the year, plague infection was found in wild rodents or their ectoparasites from 9 counties of California and 1 county each in Oregon, Kansas and Texas. The proved area of infection in wild rodents in the western United States was extended further east by positive findings in tissues from a prairie dog, and in a pool of fleas from these animals, in Scott County, Kansas.

Details of these field surveys are given in a table. It is emphasized that the reports "are at best, essentially sampling procedures" conducted by some six or seven field units of the U.S. Public Health Service in 12 states. A hunting area in the field usually covers some 5 to 25 miles.

Plague infection was proved during the year in tissue specimens or ectoparasites from species of ground squirrels, chipmunks, field mice, grasshopper mice, white-footed mice, rats, kangaroo rats, prairie dogs and a cottontail rabbit.

H. J. O'D. Burke-Gaffney

HOEKENGA, M. T. **Plague in the Americas** *J Trop Med & Hyg* 1947, Oct, v 50, No 10, 190-201, 3 figs (1 map) [Numerous refs.]

At the beginning of this review are a most useful map and a most useful table. The former shows throughout the Americas in differential shading the areas of human and sylvatic plague respectively. In the latter there are set out countries in the American continent where human cases of plague were first reported, the source of original infection, the year in which the last human case was reported and other useful data. Most of the events given in short summaries for the separate countries have already been published. Two factors in the perpetuation of plague in wild rodents are noted for the readers' attention: (1) chronic or latent infection of the rodents, demonstrated especially in squirrels (*Citellus beecheyi*) by organ pool methods, and (2) lengthened infectivity of fleas for periods such as five months and even 396 days. Some special clinical manifestations are commented on, while therapy is treated under the headings: sulphonamides, penicillin, streptomycin and serum. Several new control methods are being developed, among which the rodenticides  $\alpha$ -naphthyl thiourea ("Antu"), carbon disulphide and sodium fluoracetate ("1080") have been found efficient. As a pulicide, DDT applied with "1080" is probably the method of choice in epidemics. Prophylactic immunization fell into disrepute in Latin America but has again taken its place as a control measure. It appears to have taken the form of a killed vaccine grown on agar at room temperature. Abundant references to the literature for all the countries separately are provided.

W. F. Harvey

BARRETO, J. de B. & DE CASTRO, A. **Aspectos epidemiológicos da peste no Brasil** [Epidemiology of Plague in Brazil] *Mem Inst Oswaldo Cruz* 1946 Sept, v 44, No 3, 505-27, 2 coloured charts [28 refs.] English summary

Epidemiological data which could be usefully comparable have not been available in Brazil for very long. They have, however, increased in usefulness during the years since 1941, when progressive improvement in the prophylactic service has taken place, and especially since 1943. Some of the increase in plague, manifest in 1944 and 1945, may have been due to the more accurate

record of the disease. Laboratory diagnosis has been one of the factors in the accuracy these laboratories were 6 in 1943 and now number 21. A classification of plague cases was adopted with categories (a) positive, (b) suspected and (c) negative. Some of the older data were salvaged and kept under these headings, so that tables are presented from about the year 1891 onwards. Plague was first recorded as entering Brazil in 1899. Various tables are given by the authors illustrating epidemiological and clinical variations. The first table is an important one set out in 3-year periods in incidence 1934-36 1 247 cases 1937-39 301 cases 1940-42, 659 cases (shown elsewhere as 680) 1943-45 412 cases, revealing a decline coincident with the Federal Government's initiation of a campaign against plague in the east Brazil—the focal plague area of the country. The principal focus has been Pernambuco with 40 to 50 per cent. of the cases in the triennia investigated. Plague as a whole and this is a very interesting point, has shown three distinctive periods since its entry. In the first period, 1899-1908, plague attacked the principal ports, to pass in the second period to the cities of the interior. In the third period, which continues to the present day, plague is tending to disappear from the cities and to localize itself endemically in rural areas.

The population of the north-east of Brazil is mainly occupied in the cultivation and disposal of cereal crops, cotton, manioc and a castor oil crop. These crops are stored in the houses and, together with the accession of dirt, become an attraction and shelter for rodents and their flies.

In the quinquennium 1941-45 there were 749 cases of plague, for three of which there is no information. Many tables deal with the remaining 746 cases. Treatment was developed on modern lines and the sulphonamide drugs proved their efficacy while penicillin was discarded. In the tables furnished, care is taken to show that the percentages calculated were tested for statistical significance. Sulphadiazine was administered without plague serum in doses of 12 to 14 gm. daily for the 3 first days and of 8 to 10 gm. daily on subsequent days. The figures for laboratory diagnosis in the 749 cases, after deduction of 78 (10 per cent.) cases where this was impossible, show 342 (51 per cent.) confirmed positive while 329 (49 per cent.) were negative, although the latter were recorded as positive on clinical and epidemiological grounds. Medical opinion expressed disapproval of gland puncture as a method of diagnosis and recommended an increased employment of haemoculture, and inoculation of blood direct into the peritoneum of guinea-pigs. The method of choice for laboratory diagnosis *post mortem* was digitation to obtain bone marrow. This or gland juice or blood, was preferably sown in full-culture sulphate agar and thus despatched to the laboratory.

The vector of major epidemiological responsibility remains in Brazil as *X. cheopis* (the *X. brasiliensis* of the temperate zone) where *X. brasiliensis* is the vector. Short chapters are devoted to the epidemiology of the disease and to questions regarding susceptibility of lower animals to the infection.

The greater part of the book is concerned with various aspects of the epidemiology of the disease, particular attention being devoted to the vector *Phlebotomus papatasi*, the development and bionomics of which are described in some detail. These data are used as a basis for sanitary control, including methods of protection and destruction employed against these insects, which are described. The systematic application of these measures for the control of sandfly fever has already resulted in a marked diminution of all the diseases described in Sebastopol. A separate chapter deals with the epidemiology of sandfly fever in the region of the Black Sea.

This book, which provides information regarding sandfly fever in the subtropical diseases, is found on the 3 subpopulations of *R. rattus* parasitized by *X. brasiliensis*. The incidence of *X. brasiliensis* increases with the incidence of *R. rattus* (Alfaeus, 1941). Infection of sandfly fever has already resulted in a marked diminution of all the diseases described in Sebastopol. A separate chapter deals with the epidemiology of sandfly fever in the region of the Black Sea.

ad, G Caractères des cultures secondaires obtenues par l'action du bactériophage sur le bacille de la peste A propos des mutations du bacille pesteux en bacille pseudo-tuberculeux [Secondary Cultures obtained by Bacteriophage Action on Plague and Mutation to the Pseudotuberculous Bacillus] *Ann Inst Pasteur* 1947, July, v 73, No 7, 642-9, 2 figs

argument that *P pseudotuberculosis* is only a variant or mutant of *P pestis* tries to make its appearance Girard's own experience is wholly opposed to this idea If, however, a bacillus is found which ferments glycerin and can also to ferment rhamnose, that bacillus if it has been isolated as a plague bacillus becomes of necessity the pseudotuberculosis bacillus (of Malassez and others) That this has been done by obtaining secondary colonies after phage action on *P pestis* is claimed especially by Russian workers Only once has Girard had occasion even to record what seems to have been a mutation of the plague bacillus under bacteriophage action It was in a fatal case of plague caused by bacteriophage, the organism isolated after death, in sharp contrast to that isolated from buboes before death, produced only lesions of chronic type in the test guinea-pigs It was, however, still a plague bacillus That explanation then is to be given of the antinomy? Girard points out that plague bacilli of sylvatic plague origin do acidify glycerin and if they do possess one of the peculiar characters of the pseudotuberculosis bacillus, it is reasonable to suppose that further deviations from type might, say under the action of bacteriophage, bring about the transformation Plague strains isolated from wild rodents, Russian spermophiles of the Steppes, ground squirrels in California and sometimes South African gerbils are the strains in question which are confronted, perhaps, by two differing groups of bacilli, the murine, which is the non-deviating plague bacillus, and sylvatic bacilli Girard concludes that extracts or filtrates of plague cultures are toxic for rats and mice whereas those of Malassez's bacillus are not, and that this test might now be brought into operation in order to clear up what is still obscure in the epidemiology and prophylaxis of plague

W F Harvey

11, A da Costa & HATHAWAY, C R Pulgas Bibliografia, catálogo e lista de animais por elas sugados [A Bibliography of Fleas and their Animal Hosts] *Monografias do Inst Oswaldo Cruz* 1946, Dec, No 4, 522 pp 1946 Rio de Janeiro Imprensa Nacional

This large monograph comprises first a bibliography of books and papers on fleas, arranged chronologically, the first work quoted is dated 1544 and the last 1944 This is followed by a catalogue of the fleas of the world, the first of which is an index arranged according to families, subfamilies, genera and species The catalogue itself occupies some 240 pages, and for each species or subspecies is given extensive information (with references) on synonymy, and information on geographical distribution and on the species of animals which act as hosts

This is followed by a section of over 80 pages in which the animal hosts are listed in scientific order, with the fleas found on each species tabulated under the species A general index to the whole work occupies over 100 pages Species are not described, but the work does not claim to be more than a catalogue, and it is, indeed, an admirable compilation which should prove to be most useful for reference The authors have largely followed the classification of WAGNER, as modified, in relation to the fleas of North America, by RYLAND & FOX [this *Bulletin*, 1943, v 40, 841] For the nomenclature of the mammal and bird hosts the authors have followed well-recognized authorities

The work that has been put into this volume must have been very great indeed. There are a lot of fleas, and it is a solemn thought that, according to HARRY [this *Bulletin*, 1939 v 36, 310] any one of them is a potential vector of plague.

Charles Wilcocks

MEYERS F. M. Diagnostische moeilijkheden bij pest. [Diagnostic Difficulties in Plague.] *Med. Maandblad Batavia*. 1947 Aug. No. 13, 24, 3.

Difficulty in diagnosis of plague is frequently encountered by the clinician and epidemiologist having insufficient experience. The author instances as one example the case of several members of one family admitted simultaneously. The father had clinically and bacteriologically proved plague. One child had fever with small glandular swelling in both groins which were not typical buboes and were negative on gland puncture. The second child had moderate fever was mildly ill and had no buboes. All three recovered. There follows detailed description of two patients admitted as suspicious cases of plague, of whom one proved to be suffering from an anaerobic streptococcus septicaemia and the other from atypical pneumonia, probably due to the Friedländer bacillus. Enlargement of lymph nodes was a striking symptom in both cases and both had a periorbital oedema.

IV F Harry

## CHOLERA

MONTHLY BULL. MINISTRY OF HEALTH & PUB. HEALTH LAB. SERVICE (DIRECTED BY MED. RES. COUNCIL). 1947 Nov v 6, 196-203. Cholera. A Note by Medical Officers of the Ministry of Health.

A useful summary of the disease and its control.

CHRONICLE WORLD HEALTH ORGANIZATION 1947 Oct., v 1 No. 10 141-5. Cholera in Egypt.

This declaration of international health policy is an important, wise document of precautionary measures against epidemic disease as a whole, although directed against cholera in particular. The statement that, 'There is reason to believe that a century ago a similar epidemic could not have been checked, does not perhaps quite imply that it would have been checked in this century. A note of caution is sounded against measures of panic instituted in the name of precaution, even if they are only overprecaution, such as the complete closure of frontiers. In that example, much would depend on the type of frontier and the possibility that it would only provoke clandestine violation and thus promote the very occurrence legislated against. The argument, of course, can be applied to nearly all prohibitions if they can be or are, evaded.'

All sanitarians are anxious to put into force immediate measures to counter immediate public dangers and the summarized list of commands here set out, twenty-eight in all, should be a very valuable guide in any communicable epidemic. It follows the usual lines and will, doubtless, be transcribed and put into practice by responsible authorities. The summary may be still further abbreviated as (1) Isolation and observation of patients, contacts and local inhabitants. (2) Accelerated and enforced sanitary measures for disposal of refuse and defects. (3) Active and continued disinfection of dwellings, food and water. (4) Prohibitions on congregation and traffic of people, on the use of suspect or non-disinfected food and water on the use of public conveniences.



or drainage systems with free communication into distributive water (5) Immediate inoculation of contacts and mass inoculation of entire populations at risk

Discussions have taken place among experts with all the evidence of friendly international cooperation. Most of the opinions expressed have been on traditional lines. [One would have welcomed also some opinion that the opportunity should be taken, internationally, to investigate—traditional views for their validity, their dependence on unconscious selection of data, their statistical significance, the question of endemicity, prescribed measures, not only for their efficacy but their degree of efficacy, by definitive search the existence of negative instances, and the use of some form of alternate case method. If sanely presented, such suggestions might escape the accusation of being inhumane and qualify for statistically-scientific status.]

Conventions which are now recommended are “(a) surveillance for travellers adequately protected by vaccination, (b) surveillance and medical examination for those who have not been vaccinated”

These are very reasonable, and would presumably be accompanied by the recommendation for continued research into their foundation

W F Harvey

- i LANCET 1947, Nov 8, 694-5, 1 chart **Epidemiology of Cholera**
- ii. ABDOU, S **The Cholera Epidemic in Egypt Mode of Spread** *Lancet* 1947, Nov 8, 696-7, 2 figs
- iii. LANCET 1947, Nov 8, 697-8 **Anti-Cholera Measures in Egypt, from a Correspondent in Egypt**

i With the appearance of epidemic cholera and its threat to the valley of the Nile and the deltaic area, attention is inevitably directed to India, the traditional home of cholera. The Yangtse valley is too far distant to be considered in this connexion. It is not, however, the Ganges valley which is mentioned in this discussion, but the Punjab, where epidemic cholera started on August 15, 1947. The epidemiology of cholera was dealt with in a general and Indian sense by Sir John Taylor at a recent meeting of the Royal Society of Medicine. Upwards of 200,000 persons die of cholera in India every year. The routes of spread from this focus are (1) *via* Afghanistan to Persia and S E Russia, not now a major danger (2) *via* Iraq, Syria and Turkey to the Mediterranean, and (3) by the Red Sea to Egypt. Egyptian cholera is, or has been, linked with the annual pilgrimage to Mecca, but effective quarantine measures have, since 1912, eliminated this source of infection. Cholera patients and cholera contacts are probably the main source of cholera infection, apart from short-distance transmission extracorporeally, and both patients and contacts may excrete vibrios for about five days. The Egyptian epidemic, having reached a peak, should, like other epidemics, prophesies Sir Leonard Rogers, now die down though with some prospect of recrudescence next year. Among public health measures to be imposed in Egypt was, said Dr Melville Mackenzie, surveillance “on air passengers who had spent nights in Egypt”. The rapid advance of air travel and the shortening of time involved seem to demand a significant alteration of quarantine measures, based as they have been upon an incubation period for cholera of five days and an average excretion of vibrios also for five days. Identification of the cholera vibrio was dealt with by Mr Bruce White and especially of the three types of cholera vibrio, described as “original, intermediate and variant”. These variants or sports are transmutable, but not in the course of infection. Transmutation of non-pathogenic vibrios is another question altogether.

H. Dr Abdou deals with the course of the present epidemic in Egypt and contributes most interesting details. It started in El Kerdin, a town of 15,000 inhabitants in the date-growing province of Sharakeh. Perhaps the most important point to note regarding the population is that it has been augmented by some 6 000 immigrants settled there to work in British camps, and by 9 000 others during the date season. No correlation between the present epidemic and the British forces is admitted by the authorities. In connection with the spread of the epidemic there is mentioned the case of an old woman in El Kerdin who contracted cholera and who sent her grand-daughter to her mother in Demouh with a present of dates on October 1. The mother developed cholera and so the epidemic received its further impetus into the province of Dakahlieh. Dates and escaping settlers are incriminated as the agents of spread of cholera. It seems to have been proved that the cholera vibrio cannot live in compressed dates, but that it can live for some time on the skin of ripe dates. It is interesting to find a brief reference to the report of a medical commission sent to investigate the first cases of cholera in this region in the 1893 epidemic — Clinical and bacteriological examination has proved that the disease prevailing at El Salhieh is a gastro-enteritis due to the over-eating of dates and salted fish. [Experience of cholera outbreaks in the riverine delta of Iraq during the date season in the first world war may be recalled.]

III. In this Egyptian epidemic, the main water supplies do not appear to have played any part in the spread, but the badly constructed shallow wells have been a factor in so far as the disease has been water-borne. It is because of their better water supplies and hygienic conditions that Cairo, Alexandria and the other big cities have largely escaped infection. The number of reported cases including suspects from Sept. 23 to Oct. 21 reached 8,308 with 3,230 deaths (39 per cent.) It seems to be too early yet to judge of the value of the newer methods of treatment employed, but restoration of the depletion of water, and presumably salt, is regarded as a sheet anchor. The prophylactic value of vaccination seems to be fully confirmed" while experience with sulphamides has been on the whole disappointing. A huge campaign is being carried out to vaccinate the whole population of Egypt. A vigorous use of DDT was instituted to combat the fly menace. It may be expected that still closer analysis of this epidemic will receive publication and may help to clear up the constantly recurring problems of distant transmission, endemicity and the variant vibrios.

W. F. Harvey

Blair-Johnson is sounded against measures par les vibrations non proliférantes  
of precaution even if they are only over-riding Vibrios.] The Inst. Pasteur  
closure of frontiers. In that example, ma (13 refs)  
frontier and the possibility that it would c...proliferating vibrios, suspended in  
and thus promote the very occurrence —(1) The speed of fermentation of glucose  
course, can be applied to nearly all — and of titratable acidity for time in parallel  
All sanitarians are anxious to consumed, is more feeble in aerobiosis than in  
immediate public and it is especially marked with active aeration.  
twenty-eight in confirmed the presence of CO<sub>2</sub>, acetic acid, formic  
epidemic. The succinic acid found among the products of  
put into the cholera vibrio are derived mainly from the  
abbreviated medium. (3) Quantitative studies have shown  
that our metabolism do give rise to glucose consumed, is variable under aerobic and  
the findings for washed & active It could not be used to differentiate between  
Sept 73 v. 9 885-99 + figs El Tor except under rigorously standardized  
of pH 8 and pH 6 of F Harvey

GALLUT, J Sur l'utilisation du glucose par le vibron cholérique en aérobiose forcée [Utilization of Glucose by the Cholera Vibrio under Forced Aerobiosis] *Ann Inst Pasteur* 1947, July, v 73, No 7, 650-59, 2 figs [13 refs]

Gallut pursues his researches [this *Bulletin*, 1943, v 40, 910, 1946, v 43, 129, 1947, v 44, 421 and 660] on the metabolism of the cholera vibrio and finds that both the toxic fractions are liberated in non-aerated glucose media. It follows that the utilization of glucose by combustion instead of fermentation has no effect on the liberation of toxin. His researches lead him to insist that the differences in the morphology of the vibrios as well as in their chemical structure require continued study before concluding that cultivation under the restraint of aerobiosis in glucose media will lead to increase in antigenic power, that is, to an improved cholera vaccine. The argument is, in fact, for study of the natural biological mode of growth of the cholera vibrio as it occurs in the human intestine, with a view to obtaining effective antigen for immunization.

Gallut finds advantage in using heated agar-grown, aerated-culture, suspension [LINTON and JENNINGS this *Bulletin*, 1945, v 42, 378, 379] as well as ordinary peptone water culture for comparison of the chief characteristics of his cultures of the cholera vibrio in glucose media, which are strictly aerobic and non-aerated. These characters are set out in a table.

Some characters of the cholera vibrios according to the method of cultivation  
(24 hours at 37°C)

	Culture in Buffered Glucose		Culture in Normal Peptone Water	Emulsion of Culture on Agar (Vaccine)
	Aerated	Normal		
limits (mv)				
Upper	+81	+150	+150	—
Lower	+42	-200	-250	—
limits				
Upper	8.32	8.0	8.2	8.0
Lower	7.05	6.6	7.6	—
vibrios per cubic centimetre				
milligramme (dry)	0.909	0.240	0.914	0.750
Number $\times 10^6$	4.848	1.280	4.874	4.000
glucose broth (per cent)	1.48	0.33	—	—
total nitrogen (mgm per cc)				
fluid	0.109	0.150	3.523	—
vibrios	0.063	0.024	0.109	0.106
nitrogen content of vibrios (per cent.)	7.0	10.1	13	15
antigen (mgm per cc)	0.137	0.030	0.065	0.035
nitrogen content of vibrios (per cent.)	15.0	12.5	7.1	4.6
nitrogen content of O antigen (per cent.)	2	—	5	5

work confirms the adaptability of the cholera vibrio, which is normally facultative anaerobe, to a strict aerobiosis during the phase of growth. It utilizes glucose in aerated media at pH 7 to 8 and at slightly positive

oxidation-reduction potential ( $E_{\text{H}}$  0 at 100 mv) by combustion instead of fermentation.

W F Harvey

See also p. 180 GOODYEAR & BRAND. The Successful Treatment of Acute Renal Failure by Peritoneal Irrigation.

BURROWS W MATHER, Adaline N ELLIOTT Marian E. & HAVENS, Imbelle. Studies on Immunity to Asiatic Cholera. III. The Mouse Protection Test. *J Infect. Dis.* 1947 Sept.-Oct. v 81 No. 2, 157-74 [30 refs.]

In newer methods of measuring degrees of immunity actual protection is expressed in terms of the proportionate survival of the test animals. The old measure of agglutinin titre is no longer favoured as a real index of the efficiency of vaccine or of serum. Guinea-pigs are costly when large numbers have to be used and it seems reasonable to make trial of the mouse yet mice are relatively resistant to the intraperitoneal inoculation of cholera vibrios in broth or saline suspensions. The incorporation of commercial granular mucin in the inoculum has, however, proved successful in overcoming the resistance of mice. The present experiments, which are very completely controlled and will be a source of reference for workers in the subject must be read in entirety.

As the passive protection test was more useful than the active, it has been studied in greater detail. Vibrios for inoculation were maintained by weekly subculture on blood veal infusion agar and preserved frozen or in lyophilized culture for inoculation they were measured as dry weight (2,000 million = 1 mgm.) Mice were inoculated intraperitoneally from suspensions of 24-hour culture at a concentration of 8 to 14 mgm./ml. and in a dose of 0.2 ml. of the dilutions made from it. The mice were observed after the challenge inoculation for 72 hours but only deaths up to 48 hours (which were less erratic than those up to 72 hours and showed sharper end-points) were taken into account in calculating LD<sub>50</sub> doses.

In the passive protection test the mice were challenged 6 to 24 hours after intraperitoneal inoculation of the rabbit immune serum. It was not worth while using a normal serum control and the number of LD<sub>50</sub> doses used was found from the ratio of the LD<sub>50</sub> of immunized mice to the LD<sub>50</sub> of untreated mice.

An important pronouncement is that in a sense the fatal infection of the mouse with cholera vibrios suspended in mucin is a highly artificial one, and it is not unlikely that the virulence of many common saprophytic (?) strains can be similarly enhanced. This is due, in part at least to the amount and toxicity of bacterial substance of the proliferating bacteria. The findings of this very technical paper are that (1) A standard

fold increase method of titration is not practical, but if antibody can be expressed as ratio of the LD<sub>50</sub> dose for immunized to the control normal mice within reasonable limits (2) Only a 10-fold increase in protective titre was significant a 10-fold antibody may be in part anti-endotoxin and O agglutinin. Little or no justification is between the experimental infection and human generalized bacteraemia in the latter the bowel with only minor and rare invasion of

# AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

NELSON, E C **Alcoholic Extract Medium for the Diagnosis and Cultivation of *Entamoeba histolytica*** *Amer J Trop Med* 1947, Sept, v 27, No 5, 545-52

A new medium for cultivating *Entamoeba histolytica* is described. It consists of an alcoholic extract of chopped tissue (guinea pig liver, cat intestine, egg yolk or almost any animal tissue), in the proportion of 1 part tissue to 9 parts of 95 per cent alcohol. The spirit is driven off by warming on a water-bath, and the residue is then mixed with melted 2 per cent agar buffered at pH 7.4 in 0.5 per cent saline. (The agar solution is in the proportion of two to one of the alcoholic extract.) The tubes are put up in a steep slant and an overlay solution of 0.5 per cent saline, buffered at pH 7.4, is added to each tube. Finally a loopful of rice starch is introduced into the medium at the same time as the inoculation.

A lump of infected faeces, the size of a pea, is placed in the tube, and subculture is made after 24 to 48 hours. Most intestinal protozoa grow in the first culture, but *E. histolytica* is the only parasite which survives in the later ones. The culture can be maintained for many months or years by weekly subinoculation.

The method can be employed as a routine diagnostic procedure, and gives better results than the direct methods. P C C Garnham

CHNEIDER, R F & SHIELDS, G W **Investigation on the Transmission of *E. histolytica* by Cockroaches** *Med Bull New Jersey* 1947, Oct, v 7, No 2, 119-21

The authors, working in Talara, Peru, made cultures of the legs and intestinal contents of 100 cockroaches (species not identified) in a search for viable cysts of *Entamoeba histolytica*. They used *Entamoeba* medium (Difco), to slants of which were added before use a mixture of 1 part of human serum in 6 parts of saline, sufficient to cover the surface. A 5 mm loop of rice powder was added to each tube. After incubation at 37°C for 48 hours, the "rice serum" was examined for the presence of *E. histolytica*.

No *E. histolytica* were found in specimens from the legs of the cockroaches, they were found in 7 per cent of the cultures from the intestinal contents. The authors conclude that food and utensils can be contaminated by viable forms of *E. histolytica* from the faeces of cockroaches and that the common cockroach can be incriminated as a carrier of *E. histolytica* in Peru.

H J O'D Burke-Gaffney  
RITA, G **Contributo allo studio della sierodiagnosi nell'amebiasi [Sero-diagnosis of Amoebiasis]** *Riv di Parassit* Rome 1947, June-Sept, v 8, Nos 2/3, 113-18 English summary

With an antigen prepared from blood and mucus of a case of acute amoebic dysentery by addition of seven volumes of alcohol and filtering after keeping at 45°C for fifteen days, complement-fixation tests were carried out on 63 cases of amoebiasis. A positive result was obtained in 92 per cent of the cases. It was found, however, that the antigen reacts with Wassermann-positive sera, and therefore negative sera are alone of value in the amoebiasis tests. C M Wenyon

RUDOLPH A M & BRAUDO J L **Amoeboma of the Large Bowel with a Review of the Literature** *Clin Proc Cape Town* 1947, Sept, v 6 No 7 287-91, 2 figs [12 refs]

BRAS G. Amoebiasis van de vagina. [Amoebiasis of the Vagina.] *Med. Maandblad. Batavia*. 1947 Sept. No. 14 200-61

The English summary appended to the paper is as follows —

Description of amoebiasis of the vagina, the portio uteri and the left labium majus in a 20 year old Javanese woman in a state of cachexia due to nutritional deficiency and intestinal amoebic dysentery

SHRAPPEL, R. C. Oral Emetine in the Treatment of Intestinal Amoebiasis. *Am. J. Trop. Med.* 1947 Sept. v 7 No 3 527-44

The drug used in this study was emetine hydrochloride, prepared by Eli Lilly Co., enclosed in encoats or enteric-coated tablets, administered orally. Each tablet contained one-third of a grain of alkaloid, designed to release emetine into the lower bowel approximately 3-4 hours after ingestion, thus avoiding the emetic effect of its presence in the stomach and upper intestinal tract. A total of 30 cases of intestinal amoebiasis were treated in this series, in age groups ranging from seventeen months to 66 years. These comprised acute and chronic dysenteries, as well as carriers.

No selection of cases was made, except that none was included if emetine hydrochloride subcutaneously had already been begun.

The standardized dosage schedule was as follows —

*Children* One tablet ( $\frac{1}{3}$  grain) orally three times daily for 12 days. Total, 12 grains of emetine.

*Adults* Two tablets ( $\frac{2}{3}$  grain) orally three times daily for 12 days. Total, 24 grains of emetine.

It was suspected that some tablets might pass unchanged through the intestinal canal, and this was found true in two cases in which tablets were seen in the rectal lumen during a proctoscopic examination.

The routine observed comprised daily examination and culture of stools, urine examinations, blood measure readings, complete blood counts every three days and proctoscopic examinations before and after treatment.

The children varying in age from 15 months to 9 years, comprised two cases of acute dysentery, two chronic and one carrier cases. All presented the picture of secondary anaemia and harboured other intestinal parasites, particularly helminths. They were given vermifuges and purges in addition to oral emetine. One who was critically ill, and whose haemoglobin percentage was less than 10 per cent. required two blood transfusions.

None of the patients vomited or showed toxic manifestations during emetine treatment. The amoebae disappeared between the third and fifth days. Moderate diarrhoea, with pus cells in the faeces, was checked by sulphaguanidine in one case. A noteworthy side effect was the expulsion of large numbers of *Trichuris trichiura* in two patients as the result of oral emetine.

Twenty-five adults aged from 18 to 66 years were treated with two tablets of emetine three times daily for 12 days. They comprised 6 cases of acute dysentery, 13 of chronic and 6 of the "carrier" state.

Toxic symptoms were absent. Diarrhoea in the acute cases subsided and the number of stools was reduced to 2 to 3 daily. Abdominal cramps and tenesmus likewise subsided. Trophozoites of *E. histolytica* had disappeared on the third day but cysts were found as late as the sixth.

*Amoebic ulcerations of the rectum underwent steady healing* In one patient, residual ulcers responded to sulphadiazine.

The author re-examined 24 of 30 cases after a lapse of 2-6 months.

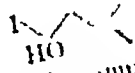
The five children were re-examined 4 to 8 months after treatment. All appeared cured. The blood picture showed marked improvement of the secondary anaemia. Nineteen of the twenty-five adults were followed up for

two to nine months. There was only one failure in this series. All expressed themselves as feeling quite well. No cases of extra-intestinal mycobiosis were encountered.

It is claimed that though the present series is small, oral emetine, in the form employed, is easy to administer, does not produce toxic symptoms, and gives effective results.

ALDRICH E. C., FAVIER D. I. & GORDON F. S. The Metabolism of Chlorofon using Radioactive Iodine. *Proc. Roy. Soc. Med.* 1947 Sept. 27 No 5, 553-60-61-62.

This elegant piece of work deals with the metabolic fate of chlorofon, (8-hydroxy-7-halo-quinoline-5-sulphonate) which has been



widely used in the treatment of mycobiosis. In the sample used, stable iodine was replaced by radioactive iodine (I<sup>131</sup>) with a half-life period of 8 days, and details of its preparation are given. Radioactivity was measured by means of a Geiger-Müller counter with a uranium preparation as standard, and details were checked against a known weight of radiochlorofon. The drug was given orally to seven fasting subjects, none of whom had mycobiosis in single doses of 100 to 400 mgm. so that 0.5 mlicurie of radioactivity was not exceeded. Blood was collected up to 8 hours after administration of the drug, and urine and faeces were collected for 2 and 7 days respectively. After the blood was freed from protein, measurements showed that activity was maximal 2 hours after ingestion and declined gradually to a negligible level in 8 hours. Part of the activity was due to iodide formed by degradation of the drug. In the thyroid region activity was noted for approximately one day. The urine was separated into two fractions by chemical means, one containing all the activity of chlorofon and iodide derived from it, and the other that of radiochlorofon alone. The amount of chlorofon excreted in urine and the extent to which it was degraded could thus be ascertained. A marked excretion occurred during the first three hours after ingestion and gradually tailed off; the total voided during the period of observation being about 12 per cent of the administered dose, of which 7.4 per cent was unaltered chlorofon. The amount of iodine split from the parent substance increased as time went on. For 24 to 48 hours and in aliquot specimens, the samples were dried at 85-90°C for the examination of faecal of 5 mgm of the powder obtained was used for measurement of radioactivity. The amount recovered in faeces varied from 50-60 per cent of the dose given. When added to that from urine, the total excretion was approximately 70 per cent of the total dosage. The authors suggest that the incomplete recovery is due to failures in technique rather than to storage in the body. It is clear from the results that absorption of chlorofon does occur fairly rapidly to the extent of 12.9 per cent of the administered dose, but clinically significant blood levels are not attained.

J. D. Fulton

PRAMANIK, S. Balantidiasis [Correspondence] *Brit. Med. J.* 1947 Nov 15, 794.

Referring to SHUK-SHUK's article on the treatment of balantidial dysentery [this *Bulletin*, 1948, v 45, 84] the author has administered  $\frac{1}{2}$  gram (11 mgm) of bimodide of mercury intramuscularly to a patient suffering from this disease.

The illness had lasted for three months as many as 20 to 30 stools being passed a day. Four days later the stool examination was negative but the infection was repeated. Two subsequent examinations were negative, the patient then reporting the passage of two or three stools per day. C. M. Weryns

## RELAPSING FEVER AND OTHER SPIROCHAETOSIS

KERVAN P. Recherches sur la sensibilité du poulet à *Spirochaeta duttoni*. Absence d'immunité du Pigeon infecté contre *Spirochaeta gallinarum*. [Researches on the Susceptibility of the Pigeon to *Spirochaeta duttoni*. Absence of Immunity against *Spirochaeta gallinarum* in Infected Birds.] Bull. Soc. Path. Exot. 1947 v 40 No. 5/6 152-5 2 charts.

Using a strain of *Spirochaeta duttoni* originally isolated from a case of relapsing fever at Dakar the author studied the behaviour of this spirochaete in fowls.

It was found that fowls varying in weight from 525 to 1 400 gm. when inoculated intraperitoneally with the blood of a rat containing this organism, showed a rise in temperature on the 4th day associated with the presence of very numerous spirochaetes in the circulation for one to two days. With the use of blood containing visible spirochaetes it was possible to maintain the strain by passage in fowls.

The organism does not persist in the brain of the fowl and even in the blood seems to lose its infectivity for the white rat.

Seven fowls infected 3 to 5 months previously with *S. duttoni* were inoculated with *Spirochaeta gallinarum* and all showed numerous spirochaetes in the circulation, but recovered from the infection. E. H. Ellis

LEVADITI, C. & VALEMAN A. Effets virulicides de la streptomycine dans l'infection récurrentielle de la souris (*Spirochaeta duttoni*). Comparaison avec la pénicilline. [Action of Streptomycin in Experimental *Trep duttoni* Infections in Mice compared with that of Penicillin.] C. R. Acad. Sci. 1947 Oct. 27 v 225 No 17 769-71

The authors found that subcutaneous administration of 5,000 units of streptomycin daily for 6 days sterilized the blood of mice which had been inoculated intraperitoneally with blood rich in *Trep duttoni*. The spirochaetes were absent from the blood of the mice during the 20 days of observation, but appeared in that of control untreated animals on the day after inoculation (and presumably remained there). Furthermore, brain substance from these treated mice failed to infect clean mice on intraperitoneal inoculation. The authors had already shown (this Bulletin 1947 v 44, 718) that large doses of penicillin, administered subcutaneously, failed to destroy the residual infection in the central nervous system of mice with long-standing *Trep duttoni* infections. In the present experiments, they were able to show that in mice infected for 58 and for 84 days, administration of a total of 30,000 units of streptomycin subcutaneously prevented infection of clean mice by means of brain substance from these treated mice in from 62 to 78 per cent of cases. The brains of untreated control mice remained virulent. Mice infected for 103 days were treated with 100 units of streptomycin daily for 12 days by the intracerebral route. Brain substance, passaged 15 days after the beginning of treatment, failed to infect clean mice, but that of the untreated controls remained virulent.

In concluding that streptomycin, like penicillin, sterilized both the blood and the brain in mice infected with *Trep duttoni* the authors point out that, while



penicillin was inactive against residual central nervous infections in mice when given subcutaneously, streptomycin produced a partial sterilization of such residual infections by this route and a total sterilization when given intracerebrally

They suggest that either streptomycin penetrates the nervous tissues more readily and more intensely than penicillin, or that the residual cerebral infection is more resistant to the latter antibiotic than it is to streptomycin, investigation of these hypotheses is being carried out *H J O'D Burke-Gaffney*

HALAWANI, A On the Transmission of Relapsing Fever in Egypt *J Egyptian Pub Health Ass* 1946, Nov, v 21, No 8, 183-90

The author discusses the classification of relapsing fever and describes the results of examination of lice, ticks, bugs, fleas and blood sucking flies during the epidemic of relapsing fever in Egypt in 1945 and 1946

He notes that body-lice, head lice and their developmental stages are the chief vectors of relapsing fever in Egypt

Spirochaetes were found in the coelomic fluid of a few bugs collected from houses feeding experiments indicated that the spirochaetes were capable of surviving in the coelomic fluid, but they were not found in as large numbers as in the case of lice

No ticks were found in any of the Egyptian houses examined, nor were fleas found to harbour spirochaetes *H J O'D Burke-Gaffney*

OMAR, M El S Reinfection in Louse Borne Relapsing Fever *J Egyptian Pub Health Ass* 1946 Nov, v 21 No 8 191-4

An account of three cases

IVAN, I M & ILIESCU, G A Contributii la studiul elementelor figurate ale sangelui periferic si organelor hemato-poietice, in febra recurenta Europeana [Study of the Peripheral Blood and Haemopoietic System in Relapsing Fever] *Rev Stiintelor Med* Bucharest 1947, Jun-Apr, v 36, Nos 1/4 76-95, 3 figs [23 refs] French summary

OMAR, M El S Rare Complications of Louse Borne Relapsing Fever *J Egyptian Pub Health Ass* 1946, Nov, v 21, No 8, 195-200

The author records the study of 6,921 cases of louse-borne relapsing fever during the epidemics of 1945 and 1946 in Egypt

The commonest complication was abortion (92 per cent of pregnancies) the next commonest was bronchitis (8.6 per cent of cases) An unposing list of other complications is given and observations are made on twelve of them

*H J O'D Burke-Gaffney*

AUBIN, H, GACHAEL, ZANGERLIN, Mme & GALLO, M Les troubles mentaux dans la fièvre récurrente [Mental Manifestations of Relapsing Fever] *Algérie Méd* 1947, May, No 5, 408-16

Relapsing fever was very prevalent in North Africa in 1944-45-46 The observations under review deal with the neurotropic effects of infection with *S obermeieri* The nervous types of the disease are classified as follows —

(A) *Confusional*—A certain amount of mental confusion is common, but in some cases a severe confusional syndrome, and not merely a temporary state, was observed, the patients being in a condition of extreme prostration, with no perception of time or surroundings, unable to understand questions or to answer coherently This form can result in acute delirium accompanied by terrifying

dreams and may show sudden and violent exacerbations. In one case (a Mahomedan Algerian) attempts to commit suicide by throwing himself out of the window were noted—these were caused, apparently by dreams of a terrifying nature. In some instances a form showing very severe prostration, usually ending fatally was observed. Usually in confusional cases an anxiety state was present.

(B) *Psychical*.—Maniacal forms are common and may occur as a primary manifestation or follow on a purely confusional state or on one of confusio-mania, or on confusion accompanied by an anxiety complex. In one instance (a young soldier) confusional symptoms appeared at the time of the second febrile attack, improvement occurring towards desferescence when typical maniacal state suddenly supervened. This patient recovered after 5 electric shock treatments. In another case (an Algerian) mania, accompanied by grandiose delusions, showed itself before the onset of pyrexia and improvement only occurred after 5 months. Irritability and impulsiveness, especially amongst natives, are other important symptoms in this type—a few electric shock treatments usually suffice to bring about cure.

The depressive form is very rare, having only been seen in one instance and then following on a confusional state.

(C) *Protracted types*.—Most writers hold that such types are rare, and chronic forms have not been noted. The authors report a case in a Spaniard who became stuporose at the commencement of pyrexia, appearing to have no realization of his identity. After 7 months he recovered use of his speech admitting having auditory hallucinations—later a diagnosis of paranoia was confirmed. This condition is now of 2 years standing.

The authors describe several cases showing that mental disorder may become chronic, in some cases ending in actual insanity. Electric shock treatment appears to be of benefit in certain instances. Various types, religious mania, delusional and hallucinatory forms are described in some detail.

The time of appearance of psychoses is variable and not necessarily in the precrisis of the first febrile attack. Mental symptoms were observed during the incubation period before any signs of infection appeared, and early psychotic forms may develop into mania long after disappearance of signs of infection. It is impossible definitely to separate primary psychoses from those due to the infection.

During the actual attack, confusional conditions with dreams and an anxiety state are most common, but, as noted, the first appearance may often be in the apyrexial phase with absence of spirilla in the blood, and hence one difficulty in diagnosis.

During convalescence mental symptoms tend to appear in more or less atypical forms—delirium with sudden onset and return of pyrexia—psychological troubles of a trivial nature, perhaps delayed for several weeks or months after cessation of pyrexia.

A history of various chronic infections or intoxications is often found, especially alcoholism, which in some cases gives rise to a syndrome resembling delirium tremens, and syphilis. Five patients showed positive Wassermann reactions—one of these after an attack of relapsing fever developed a mental syndrome of continued amnesia and poverty followed by signs of a tabetic type and a spasmodic paraplegia (syndrome of Guillain and Thoen).

[Some authorities hold that relapsing fever does not give a positive W.R. in the blood, others hold a contrary view.]

[Possible mental complications in relapsing fever are worth bearing in mind from a medico-legal aspect in regions where this disease is prevalent.]

EL-RAMLY, A H Three Papers on Louse Borne Relapsing Fever I Treatment of Louse Borne Relapsing Fever *J Egyptian Pub Health Ass* 1946, Nov, v 21, No 8, 125-49 II Splenic Infarctions *Ibid* 150-65, 3 charts III Report on 139 Fatal Cases of Louse Borne Relapsing Fever *Ibid* 166-82

The author of these three papers is Director of the Fever Hospital, Imbaba, Egypt

i This paper records the study of 856 cases of louse-borne relapsing fever, 684 of which were treated with different arsenicals and 172 were kept as control

The patients were divided into ten groups and each of nine groups was given a different treatment schedule with varying doses of NAB, Mapharsen, Mapharside and Glyvarsenyl the tenth group served as a control

Details are given of the results obtained in each group, in terms of fall of temperature, disappearance of spirochaetes, relapses and mortality details of five fatal cases are given

The final results of all the treatment schedules are shown in a table the author does not, however, attempt to analyse them comparatively, and as several factors require to be taken into account, the table should be studied in the original

ii In 3,000 consecutive cases of louse-borne relapsing fever, infarction of the spleen was found in 75 (2.5 per cent) there were 28 deaths Most of the patients were between 20 and 65 years and males predominated The condition is easily missed it occurred mostly in the original attack and first apyrexial period

In 52 cases the infarctions were simple the remaining 23 were septic

The signs and symptoms are discussed, and full details are given of four patients Arsenical drugs were not found to be of use in treatment or in preventing occurrence of infarction penicillin may prevent sepsis, if it is given early during the stage of simple infarction

iii Between January and July 1946, there were 7,379 cases of louse-borne relapsing fever admitted to Embaba Fever Hospital [this is printed earlier in the *Journal* as "Imbaba"] Of these, 273 patients died Autopsies were carried out on 139 of the fatal cases, and the results are discussed at length. It is noted that in 8 cases, foetuses of from 6 to 8 months were born prematurely, showing characteristic post-mortem signs of relapsing fever all the mothers concerned had showed the specific spirochaete in their peripheral blood, and were actually suffering from relapsing fever at the time of miscarriage

The morbid anatomy of relapsing fever, and of the complications found, is discussed and the records of 11 cases are given *H J O'D Burke-Gaffney*

HARTMANN, F W Further Observations on Leptospirosis in Micronesia *Science* 1947, Sept 26, 294

This records information additional to that given by ALICATA [this *Bulletin*, 1947, v 44 665] The investigation was carried out in this case on the island of Yap, in the Western Carolines, south and west of Guam

In Yap Town, 28 rats were trapped alive, these comprised three species, *Rattus alexandrinus*, *R. norvegicus* and a third, provisionally identified as *R. vulans micronesiensis* Pieces of kidney, removed immediately after each rat was killed by drowning, were preserved in 10 per cent formalin for several months and were then stained by a silver precipitation technique No spirochaetes were found in any of the kidney sections

The author concludes (although the number of specimens was small) that murine leptospirosis is not present in that area, possibly because Yap is geographically isolated If, however, *L. icterohaemorrhagiae* was once introduced



42 years against 32 to 66 in the Spanish-American war, this also suggests that in the more recent wars infection occurred in foci in the U S A where the infected persons had been born. Most of the patients from Louisiana have been of French origin. L Rogers

CHAUSSINAND, R Contribution à l'étude de la morphologie du bacille de Hansen [The Morphology of Hansen's Bacillus] *Ann Inst Pasteur* 1947, July, v 73, No 7, 660-65

In the course of his prolonged studies the author has distinguished four distinct morphological forms of leprosy bacilli, as follows: normal bacilli are rod shaped, sometimes with pointed ends, they are of variable length and stain uniformly by Ziehl's method. Secondly, bacilli undergoing evolution are large, occasionally branched and with thickened ends and they do not always stain uniformly. They are found especially in macules and tuberculoid infiltrations and nerve cases which are showing resistance and tending to cure. They are not found in progressive lepromatous cases. They are also present in inoculated animals showing resistance to infection. Thirdly, bacilli undergoing division are divided into two or three nearly equal lengths by small unstained transverse intervals where they divide by fission, they may show some granulation. They are never found in nerve cases not undergoing evolution and are less frequent in treated than in untreated cases; but they are present in large numbers in globi in degenerating lepra bacilli, disintegration takes place by progressive stages with the appearance of lightly staining granules in the rods, followed by gradual loss of staining power and the appearance of chains of granules, which in turn disintegrate to minute dots and then disappear. This last form increases *pari passu* with the clearing up of cutaneous cases under treatment. No proof has yet been furnished of the existence of an ultra-microscopic form.

[It may be of interest to recall that the reviewer, in 1917, recorded and illustrated increased granulation of lepra bacilli and their gradual disintegration and disappearance from nodules of the ears, with improvement under treatment by injections of soluble preparations of chaulmoogra oils (this *Bulletin*, 1918, v 11, 407)] L Rogers

CHAUSSINAND, R A propos des essais de culture du bacille de la lèpre [Attempts at culturing Leprosy Bacilli] *Ann Inst Pasteur* 1947, May v 73, No 5, 433-8 [14 refs]

This is a valuable summary of over 1,000 attempts to cultivate lepra bacilli in the course of ten years, with suggestive tests for the true organism to enable others to avoid the common fallacies of the hundred or so former workers who have incorrectly claimed success. SOULE and MACKINLEY appear to have come nearest, by obtaining minute colonies of the causative organism, but no one has obtained a series of subcultures. Readers should consult the original for a bibliography of former attempts and for a summary of the numerous culture media unsuccessfully employed by the present author. He concludes that workers have been misled through an apparent increase in the bacilli, with gradual dissolution of leprous tissue cells inoculated on media, and the carrying over of many of them on subculture. What may possibly have been a very slow appearance and increase of colonies of acid-fast bacilli with the characteristic appearance and arrangement of Hansen's bacillus may have been obtained occasionally, but subculture has proved difficult or impossible. The author advises the use of the following two tests to determine whether any apparent cultures are true leprosy bacilli or not: (1) The intradermal injection of

suspensions of Hansen's bacillus killed by heat gives negative local reactions after two weeks in lepromatous leprosy and positive reactions in tubercloid leprosy. On the other hand, similar injections of tubercle, paratubercle or Stéfanaky's rat leprosy bacilli give more or less intense positive reactions in the case of all lepromatous persons who are sensible to tuberculin. (2) When Hansen's bacilli are injected into the general body cavity of the larva of the wax moth (*Galleria mellonella*) they are phagocytized by giant cells, but are digested very slowly so that they can be stained and easily recognized several days later in the insects. But tubercle bacilli and saprophytic acid-fast paratuberculous bacilli, formerly so frequently mistaken for Hansen's bacillus, are rapidly disintegrated and disappear from the giant cells within a few days. The use of these tests will enable the true character of any cultures obtained from the leprosy tissues to be determined.

[The larva of the wax moth *Galleria mellonella* is regarded as the guinea pig of insect microbiology and has been utilized in phagocytic studies of many bacterial species, owing to its varying capacity for phagocytic response to the inoculation of bacteria and other foreign particles. See also CAMERON *J. Path. & Bact.*, 1934 v 38 441 and STEINWART, *Insect Microbiology* 1948 568 Comstock Publishing Co. New York.—Ed.] L. Rogers

CHAUMINAND, M. Inoculation de la lèpre aux animaux. [Animal Inoculation with Leprosy Material.] *Ann. Inst. Pasteur* 1947 July v 73 No. 7 677-82.

The author summarizes in this paper ten years' experience of inoculations of animals with leprosy material. In the case of white mice subcutaneous inoculation of material containing very numerous lepra bacilli produced only local lesions and alopecia but three animals which survived intraperitoneal injections later showed scattered bacilli in the internal organs. Monkeys have also been inoculated by various routes. Intradermal and subcutaneous injections have produced local lesions only after three to five months—these disappeared again before long and left no trace nor was any multiplication of the bacilli found. Lepromatous nodules were implanted in the subcutaneous tissues, with the production of purulent lesions which healed slowly and were of an eliminative nature and not true infective lesions. However the insertion of a leprosy nodule into the peritoneal cavity did produce an infection, with the appearance of cutaneous lesions containing acid-fast bacilli—the tuberculin test was negative, but the Mitsuda was positive. Later the lesions resolved with progressive disappearance of the Hansen-like bacilli from the tissues, and the Mitsuda reaction became negative. Inoculation of lepromatous emulsions into guinea pigs by various routes gave no results, as the bacilli were eliminated more or less quickly. On the other hand, the insertion of a leprosy nodule under the skin of the nape of the neck produced a local infection.

The author concludes that the inoculation of animals with leprosy material does not produce infections of a general nature, such as would afford opportunities for testing the value of therapeutic substances used in the treatment of the human disease. L. Rogers

ORDEMAYER, M. E. Diffuse Leprosy. *Ann. Western Med. & Surgery* 1947 Aug. v 1 No. 6 225-31 6 figs.

The author has had a large experience of this dangerous and easily overlooked form of lepromatous leprosy since it accounts for as many as 60 to 70 per cent. of all lepromatous cases in parts of Mexico where he works and 17 per cent. in other Mexican areas. As the disease develops slowly with indefinite and not easily recognized symptoms, it easily escapes detection, yet is highly

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infective After discussing the differences between lepromatous and tubercloid types of leprosy, the author describes the pure diffuse lepromatous form. Cutaneous nodules are absent and there is a diffuse infiltration of the skin of the whole body and a peculiar lepra reaction described by R LUCIO as an *erythema necroticans*. Lucio called this form "spotted" or "Lazarine" lepra as early as 1851, and LATIPI studied it further in Mexico in 1937. The unique lepra reactions appear three or four years after the onset of this type of the disease as tender and painful erythematous and slightly infiltrated small macules on the extremities and face, which develop central necrosis leaving superficial, sharply circumscribed atrophic scars, these lesions are illustrated by five photographs. Osseous destruction may result in a saddle nose, but the eyes are not affected. The eyelashes and eyebrows are frequently lost and alopecia of the scalp may follow. Progressive weakness ensues with death, occurring after an average of eight years, the Mitsuda reaction remains negative throughout, indicating absence of resisting power. Numerous lepra bacilli are found in the diffusely infiltrated skin in all parts of the body, unfavourable reactions follow the use of chaulmoogrates or iodides.

L Rogers

TISSEUIL, J Deux types de lèpre cutanée tertiaire, dermique rouge en nappe, hypodermique blanche en nodule [Two Types of Cutaneous Tertiary Leprosy] *Bull Soc Path Exot* 1947, v 40, Nos 5/6, 147-9

The author describes red and white tertiary cutaneous leprotic lesions which he thinks are liable to be confused. The red form occurs particularly on the body in the form of extensive, isolated thickenings or nodules of a yellow or red colour showing necrosis and very numerous lepra bacilli on section, and it may cicatrize to leave white radiating scars, it tends to develop rapidly.

On the other hand, the white lesions are more frequent on the face and extremities in the form of isolated nodules up to the size of an almond, these are situated in the subcutaneous tissue and freely movable under the dermis which is pale white. They contain numerous polynuclear cells and lepra bacilli and tend to soften and discharge through the skin, leaving ulcers which heal slowly. They are easily excised and have a fibrous coating, they discharge many bacilli and have a longer duration than the red form.

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MONTESTRUC E & CAUBET P Alnhum in a Leper *Trans Roy Soc Trop Med & Hyg* 1947 Oct v 41 No 2 187-8 2 figs

A lesion of the little finger illustrated by a radiograph and a photograph

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Report of a case

## HELMINTHIASIS

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The zinc sulphate flotation technique of FAUST *et al* [this Bulletin, 1939, v 36, 144 *ibid* 1940 v 37, 62] is coming into increasingly prominent use for the concentration of ova and cysts in faeces. It has, however, the disadvantage that trophozoites of protozoa are destroyed by the repeated centrifugation.

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## HELMINTHIASIS

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(1305)

The author in Durban, compared this technique with the direct faecal film in the examination of 1,539 routine specimens of stools, derived mostly from cases of suspected amoebiasis. For the reason noted above findings for protozoa refer to cystic forms only.

The results are clearly set out in the form of two tables and a chart. One of the former shows the exact findings of six species of protozoa and six species of helminths, by the direct and flotation methods, separately and together. Conflicting results with the double techniques are also shown, together with the totals of all positive findings. The second table indicates the relative efficiencies of each method, singly and together, and includes a column showing the ratio of positive results by the zinc method to that of the direct, expressed as percentages. The chart compares graphically the proportion of positive findings, in the form of appropriately shaded circles.

Four hundred and twenty (38.6 per cent.) specimens were negative by both methods. In the remainder there was considerable variation in the total of positive findings, from 8 and 11 in the case of *Chilomastix mesnili* and *Schistosoma mansoni* to some 200 in the case of *E. histolytica* and *E. coli* and hookworms, and some 600 in the case of *Ascaris* and *Trichuris*.

For a statistical appraisal of the results, the tables should be consulted, but it may be said that, on the whole, there was a striking gain in positives for nearly every species of parasite when the zinc sulphate flotation was used. Protozoal cysts floated well, especially those of *Iodamoeba butschlii*; the absence of faecal debris made ova and cysts easy to find.

Nevertheless, some ova did not usually float well, especially those of *Ternstroemia* and *Schistosoma mansoni*; they were often found in the final centrifuged deposit.

The author calculates that the average overall gain obtained by the use of Faust's zinc sulphate flotation amounted to 179 per cent. in the case of hookworm, *Giardia* and *Iodamoeba butschlii*; it was over 500 per cent. The technique is a very valuable diagnostic aid in the examination for intestinal parasites, but the author believes that the direct film still remains the method of choice, since trophozoites may also be detected with its use. Where possible both techniques should be employed.

H. J. O'D. Burke-Gaffney

DR MELLON B. Aspects of the Natural History of Bilharzia in South Africa. Read at a Medical Congress, East London, South Africa, 1947. 6 pp. [17 refs.]

This paper read at a medical congress in East London, South Africa, is an able summary of the position as regards human schistosomiasis in the Union. *Schistosoma haematobium* is found throughout the whole Transvaal north of about 28°S. and there is a strip of country also infested, down the coast as far as Port Elizabeth. Snails capable of acting as intermediate hosts exist in areas hitherto unaffected by the disease, but the increase which is taking place in the movements of labourers may bring infection to new areas. *Schistosoma mansoni* was hardly known in the Union in 1934 but since then indigenous cases have been found in Natal, N.E. Transvaal, Central Transvaal, Eastern Transvaal, and Swaziland. This infection is apparently spreading actively having been introduced from the north.

The author remarks on the difficulties experienced in the identification of molluscs and on the scarcity of experts on the subject. In the Union, the following molluscan hosts have been found for *S. haematobium*—*Physopsis africana*, *Physopsis globosa*, *Bulinus tropicus*, *Bulinus forskalii* and (doubtful) *Lymnaea natalensis*. The host of *S. mansoni* is *Planorbis* (*Biomphalaria*)

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*pfeiffer* The author gives a list of places where these snails are found, they are much more widely distributed than the corresponding schistosomes.

The ecology of these snails has not been studied systematically, and there is a need for research on this subject. It is, however, known that snail-spawn is deposited on aquatic plants, and may be transported considerable distances on the legs of wading birds, it is also known that some snails prefer mud rich in organic matter such as faeces. There is a general impression that rivers running west in the Union are not dangerous in respect of schistosomiasis, and thus is largely true, because the rivers are in their natural state, perennial, with sandy bottoms and subject to violent flushing so that there is little true aquatic vegetation, snails do not flourish in such streams. If these rivers are dammed, however, they will become suitable for the snails.

The author gives a detailed description of the laboratory techniques for identification of cercariae from wild-caught snails, for infection of laboratory snails, and for their maintenance. These details must be sought in the original paper.

The paper ends with a warning that the great industrial development planned for the Transvaal, which will involve a large increase in population and which has already led to the impounding of water in the Vaal river, may mean a very great spread of schistosomiasis if the relevant snails become established, the prospect, if this happens, will be grim. The author also notes that African immigrants from tropical areas are not permitted to settle in urban areas, and that they therefore seek the small farms close to towns, and may infect the snails in the waters about those farms.

Charles Wilcocks

- 1 BASSÈRES, M S & PANTOJA, W P Esquistossomose — Prevalência de *S. mansoni* na população humana [The Prevalence of *Schistosoma mansoni* in Man in Part of Minas Gerais, Brazil] *Rev Serviço Especial de Saúde Publica* Rio de Janeiro 1947, v 1, No 1, 135-48, 1 fig & 1 map English summary

- 11 — & — Esquistossomose Prevalência de *S. mansoni* em Planorbídeos [The Prevalence of *Schistosoma mansoni* in Planorbid Snails in Part of Minas Gerais, Brazil] *Ibid*, 149-62 [12 refs] English summary

1 The authors examined faeces from 5,314 persons (about 15 per cent of the population) along the Victoria-Minas railway. The specimens were examined by the Stoll-Hausheer technique. Part of the route lies along the Rio Doce, and three zones were recognized. The first lay away from the river, and here the proportion of persons infected with *S. mansoni* was 0.9 per cent. The second zone lay entirely along the river, with an index of infection of 21.1 per cent. The third zone lay partly along the river, and partly away from it, where the railway diverges from the main stream, and in this zone the index of infection was 12.9 per cent. Incidence reached its peak in the age group 15-24, and was rather greater in males than in females at all ages.

The infection rates in planorbid snails (see below) varied from nil to 11.1 per cent. Details of the findings are set out in a series of tables.

11 In connexion with the investigations in man referred to in the preceding abstract, the authors examined 5,248 planorbid snails taken in the three zones. Most of the snails were *Australorbis olivaceus*, a well-known intermediate host of *S. mansoni*, but other genera were also examined, in small numbers.

In Zone I, where human infection is light, no infected snails were found, and in Zone II, where human infection was found in 11.1 per cent of 4,297 snails, chiefly in creeks, springs and ditches, and there was evidence that they may

spread from the main streams of the Rio Doce up the tributaries. The basin of the Rio Doce apparently constitutes a single unit in relation to schistosomiasis.

Charles Wilcocks

- i. MALDONADO J F & ACOSTA MAYUENTO Josefina. The Development of *Schistosoma mansoni* in the Small Intermediate Host, *Australorbis glabratus*. Puerto Rico J Pub Health & Trop Med. 1947 June, v 22, No. 4 331-73 29 figs. [Refs. in footnotes.] [Spanish version 374-404]
- ii. — & — Larval Cycle of *Schistosoma mansoni* in its Small Intermediate Host, *Australorbis glabratus*. Kuba, Habana. 1947 Mar., v 3, No. 3 69-72, 5 figs.

1. "1 The miracidium of *S. mansoni* bears a close resemblance to that of *S. haematolum*. In addition to other structures described in previous accounts, it is also provided with an anterior *terebatorium* and pairs of antero-lateral and postero-lateral papillae. What has been described by others as clusters of lateral secretory glands with their corresponding ducts, is believed to be ganglionic nerve cells and nerve tracts that run to the antero-lateral papillae. A germinal epithelium has not been observed.

"2. The miracidium penetrates into the molluscan host by actual perforation of the epiderm of the head-foot organ the tentacles, or the mantle collar. On rare occasions, a larva may gain access to the shell cavity and from there penetrate and settle in rather distant locations.

3. The snail may be simultaneously parasitized by numerous miracidia. However during the first days of infection many will fail to develop, so that the number of mother sporocysts in multiple infections is smaller than the number of miracidia that actually penetrate.

4. Implantation and subsequent development occurs close to the point of entrance. Within five hours the miracidium loses its motility and sheds its ciliary membrane. By the twenty fourth hour the germ cells in the larva begin to divide. The parasite may then be called a mother sporocyst.

"5 By the forty-eighth, many of the mother sporocysts may appear as fairly elongated, simple, thin-walled sacs full of germ cells. The body begins to develop transverse constrictions that make the parasite appear like a series of separate chambers. Beyond the second day and up to the twentieth, the sporocyst grows markedly in length, becoming an intricate organism with numerous constrictions and convolutions. Essentially however it is a long, thin-walled tube. There is no evidence of motility in the mother sporocyst *per se*. Migration of this stage through the snail tissues is therefore, highly improbable.

6. Whenever the mother sporocyst develops close to the surface of the head-foot organ in the tentacles, or in the mantle collar of the snail, a permanent tumefaction arises. The swelling becomes perceptible on the fourth day of infection and grows in size with advancing age.

7. The daughter sporocysts can be first observed within the mother form by the fourth day of infection, appearing as undifferentiated masses of cells. By the eighth day many are already elongated and motile and by the eighteenth, they begin to migrate towards the distal glandular tissues of the snail where they finally settle and grow. In heavy infections some daughter sporocysts may fail to reach such sites, developing in other parts of the host. A mother sporocyst may give rise to hundreds of daughter forms.

"8. Cercariae arise within the daughter sporocysts by germ ball formation. The first cercarial germ balls may appear while the sporocyst is still on its migratory phase. Once in its final habitat numerous other balls are produced.

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Each one of them elongates after reaching a certain size and develops a constriction at the middle whereby the tail arises. Subsequently, the other organ systems are formed and, in a few days (ca one week), the mature cercaria is ready to emerge from the snail."

" This is a shorter version of the above

OTTOLINA, C. **The Rectoscopic Biopsy by Transparency** *A New Diagnostic Method for Schistosoma mansoni* *Amer J Trop Med* 1947, Sept, v 27, No 5, 603-6

The author discusses the origin and rationale of the rectoscopic biopsy for the diagnosis of *Schistosoma mansoni* infections described by himself and ATENCIO in 1943 [this *Bulletin*, 1944, v 41, 945]

In the test, a fragment of mucous and submucous tissue from the upper half of the rectal ampulla is taken from the middle Houston valve about 10 cm from the anus in the area drained by the superior haemorrhoidal veins. This tissue is digested for 3 to 4 hours in 4 per cent caustic potash solution at 60° to 80°C, and examined microscopically after centrifugation.

The author discusses his experience and that of others with the use of this technique, and refers especially to the work of RINCON URDANETA (*Rev Policlínica Caracas*, 1945, v 14, 325). The value of the rectoscopic method compared with stool and intradermal tests is emphasized and comparative figures from the literature are given. The rectoscopic biopsy is a direct method with only a negative error and this has an advantage over indirect methods nevertheless its value would be greater if these false negatives could be avoided.

One factor which seems to influence these errors is that caustic potash digestion, although it made it easier to find eggs in light infections, involved further and harmful manipulation.

Direct microscopic examination of the fragments before digestion did not prove adequate. Many devices were tried to make the tissue fragments transparent and eventually it was found that this could be achieved by immersing them for 3 to 5 minutes in fresh water. This dissolves the haemoglobin and the eggs appear in characteristic strings. Also the living fragment absorbs water quickly and after 3 to 5 minutes becomes a watery globule. This is then compressed between two slides, a drop of water is added, the whole is covered and pressed gently and a thin transparent film can be seen. The eggs can be easily seen in the film by focussing with the lower power of the microscope at different levels.

The method is simple and rapid and, in light infections, avoids losses which may occur during caustic potash digestion. An important advantage is that normal eggs containing living miracidia are often seen by the transparency method in specimens from untreated patients. Such miracidia are killed by the digestion method. This is of therapeutic significance, as it aids in determining the course and results of treatment.

It is stated that the movement of miracidia in individual eggs can be detected with a high power without difficulty and it is even possible to puncture an egg with a fine needle to deliver the miracidium under microscopic control.

The author concludes by recording that rectoscopic biopsy by transparency presents a clinical diagnosis of *S. mansoni* in a few minutes. The high figures already obtained with the rectoscopic biopsy alone suggest a thorough revision of our clinical knowledge of schistosomiasis. [see also this *Bulletin*, 1947, v 44, 330]

H J O D Burke-Gaffney

DA SILVA, J. R. & COSTA, N. A biópsia retal no diagnóstico e no controle da eficiência terapêutica da esquistosomíase de Manson. [Rectal Biopsy in the Diagnosis and Therapeutic Control of *Schistosoma mansoni* Infection.] *Hospital* Rio de Janeiro. 1947 Aug v 32, No. 2 219-33 7 figs. [16 refs.] English summary

The authors found *S. mansoni* eggs in 13 of 100 patients sent for diagnosis of schistosomiasis by the rectal biopsy technique in only 4 of these 13 patients were faecal examinations positive after repeated search. On the other hand, in one patient faecal examination was positive and two biopsies were negative.

The authors refer to the previous work of HERNÁNDEZ MORALES and MALDONADO [this *Bulletin* 1947 v 44 330] and discuss their observations on the possibility of estimating therapeutic efficacy by the morphological study of schistosome ova found in biopsy material.

They conclude that rectal biopsy greatly simplifies the diagnosis of *S. mansoni* infections, especially where laboratory facilities are limited. It is simple, quick, without risk and does not require the detention of the patient in hospital. The paper is illustrated with seven photomicrographs showing ova that were detected. [See OTTOLIXA, above.]

H. J. O'D. Burke-Gaffney

WRIGHT W. H., McMULLEN D. B., BENNETT H. J., BAUMAN P. M. & INGALLS, J. W., Jr. The Epidemiology of Schistosomiasis Japonica in the Philippine Islands and Japan. III. Surveys of Endemic Areas of Schistosomiasis, Japonica in Japan. *Amer. J. Trop. Med.* 1947 July v 27 No. 4 417-47 7 figs.

The authors explain that their report lacks the usual historical review since for various reasons they had not full access to the Japanese literature on the subject. On the other hand, the information collected on the spot from doctors and health workers has been incorporated, and in spite of the language difficulties which were encountered, supplies data not otherwise available in published accounts of schistosomiasis in Japan. The Commission surveyed five known endemic areas of schistosomiasis, with a view to delineating the extent of these areas and gaining information which would assist in the protection of troops stationed in them. "On entering an endemic area, as much information as possible concerning the status of the disease was obtained from prefectural and local health authorities and from practicing physicians. Based on this information, certain schools in various parts of the area were selected, and a representative number of stool samples obtained from children in the higher age groups (8 to 15 years) for microscopic examination for schistosome eggs. Surveys were then conducted in various parts of the area for *Oncomelania* (*Katayama*) *nasophora*, the snail intermediate host of *Schistosoma japonicum*. When the snails were found, sufficient numbers were collected for transport to the laboratory for examination for incidence of infection.

"All stool examinations conducted by the commission were carried out with the use of the plain sedimentation technique. This technique had previously been found to be the most efficient one for practical use in the field, through research carried out by members of the commission on Leyte and other islands. The technique consisted in taking five grams of feces, stirring the sample in water, straining the material through four layers of surgical gauze into a 250 cc. conical urinalysis flask, allowing the material to sediment, and pouring off the supernatant fluid. At least three decantations were made. One drop of the final sediment was placed on a slide and examined under the microscope. In the examination of school children in Japan, the commission followed the practice of examining two 22x22 mm. cover glass preparations or one 22x40 mm. cover glass preparation from each sample. A total of 1 688 school

children were examined by the Commission in the five endemic areas, of these, 381 (22.6 per cent) were infected with *S. japonicum*. A higher proportion of males than females were found to be infected, 29.2 per cent of the boys as compared with 16.7 per cent of girls. This finding is in agreement with that of the Japanese who found a preponderance of infection in all cases amongst the male population and ascribed it to "their greater opportunities of acquiring infection."

The following summaries of the Commission's surveys show that the incidence of infection in the human population and in the snail vector varied considerably in the five areas.

(1) *Tone River Area, Chiba and Ibaraki Prefectures*—This has the lowest infection rate of any area in Japan, and only 3 out of 390 school children, examined in six localities, were found to be infected. The Commission was unable to find specimens of *Oncomelania (Katayama) nosophora*, the most important snail vector, although this species of mollusc undoubtedly occurs in some parts of the area.

(2) *The Kofu Area in the Yamanashi Prefecture*—In contrast to the Tone River area, this is the most important schistosomiasis district in Japan, and in spite of the intensive control which has been carried on since 1942, the commission found that 245 out of 458 (53.5 per cent) school children were infected. This figure is more than double that previously recorded in the same school by doctors of the Japanese Health Department, who had estimated that 24.2 per cent of the children were infected. The same Japanese Health Authorities had also examined the general population with the following results—

*Results of stool examinations for schistosomiasis carried out in the Kofu area by health authorities of Yamanashi Prefecture between May 1 1944 and April 30 1945*

Area	No Persons Examined	No Persons Positive	Per cent Positive
Control	81 031	5 026	6.2
Under control	57 013	2,983	5.2
Uncontrolled	22 862	2 583	11.3
Totals	160 906	10 597	6.6

That these figures are well below the true infection rate is suggested by the American Commission's comment that "all these examinations were made by means of a single fecal smear with what the commission regarded as inadequate equipment." The evidence obtained from the same source indicates that certain domestic and wild animals are responsible for the transmission of infection to the snail intermediate host.

The snail vector, *O. nosophora*, was found without difficulty in the Kofu Area, and of 200 snails which were crushed and examined, three were found to be infected.

(3) *The Namazu Area in the Shizuoka Prefecture*—Previous data concerning the infection in the general population between 1920 and 1926 were published in 1933, and showed that about 4 per cent of the total population were infected. Since that date, the Japanese have drained a large swamp in the centre of the area and this measure has probably materially reduced the schistosomiasis rate. In the present survey, the American Commission found 14 out of 155 (9 per cent) of the children infected with *S. japonicum*. The snail vector was localized to one area, where, out of 315 *O. nosophora* examined, 2 (0.63 per cent) were infected.

Results of examinations for *S. japonicum* infection lower animals: the tests were carried out by health authorities of Yamaguchi Prefecture between May 1 1944 and April 30 1945

Species	No. Examined	No. Positive	Per cent. Positive
Cattle	7,059	2,184	30.9
Goats	1,118	158	14.1
Dogs	353	178	49.9
Horses	987	0	0
"Rats" (probably including field mice, <i>Microtus</i> spp.)	1,707	656	38.4
Moles	66	13	19.1
<i>Mustela</i> sp.	10	9	90.0

Probably *Mustela* (skunk) stated.

(4) *The Fukuyama Area in the Hiroshima and Okayama Prefectures.*—Through the organized control work which has been carried on in this area over the past 30 years, the disease has been greatly reduced and the distribution of the small intermediate host considerably restricted. The disease is now confined to the fringes and to the centre of the area, and of 357 children examined from these areas, the Commission found 34 (9.5 per cent.) to be infected. Control measures by the Japanese had considerably reduced the numbers of *O. mesophora* which was now confined to an area of approximately four square miles. Out of 501 snails collected from this area, 19 were found infected, the percentage of infection in the snails collected from different localities varying from 0.5 to 15.8 per cent.

(5) *Kurume Area in the Saga and Fukuoka Prefectures of Kyushu.*—Considerable published Japanese data concerning the previous incidence of schistosomiasis in this area were available to the Commission, but the differences in the techniques employed and in numbers examined made it difficult to compare the results. The Japanese figures depict a steady diminution in the incidence of the disease but the present authors' examination of 328 children from three schools revealed an infection rate of 25.9 per cent., a figure which suggests that there has been little if any decrease in the schistosomiasis infection rate in this area during the past 20 years. The distribution of the snail intermediate host varied considerably *O. mesophora* being found in abundance in the areas with high human incidence of infection, and being absent from, or scanty in, areas with a low human incidence of schistosomiasis. The infection rate among the 510 snails which were dissected varied from 4 to 9.5 per cent. according to the area from which they were collected.

This paper contains references to other helminth infections which were observed in the specimens of faeces examined for the presence of *S. japonicum* on a.

R. M. Gordon

VOGEL, H. & MEYER, W. Ueber die Einwirkung von Brechweinstein, Fuadin und Emetin auf *Bilharzia japonica* und deren Eier im Kaninchenversuch. [The Action in Guinea-pigs of Tartar Emetic, Fossatin and Emetine on *Schistosoma japonicum* and its Eggs.] *Acta Tropica*. Basle. 1947 v. 4 Nos. 1 & 2, 21-53. 97-116. 9 figs. [22 refs.] English summary.

Experiments were carried out on rabbits to ascertain the nature of the effects of certain drugs on the adult *S. japonicum* and whether they would destroy eggs in the tissue of the host.



The animals were exposed to infection with a known number of cercariae, and after the commencement of egg passage 29 of the rabbits were treated with tartar emetic, 7 with foudadin, 10 with emetine and 6 were kept as untreated controls. The dosage was 2.5 mgm (intravenously) for tartar emetic, 0.11 cc (intramuscularly) for foudadin and 2 mgm (intravenously) for emetine. The dosage and intervals between doses was kept constant throughout, but the number of injections varied from 3 to 24.

*Tartar emetic*—At least 9 to 12 injections were required to cause the eggs to fail to hatch. It was concluded that after 6 injections, about half the adult worms still survived, about one-fifth survived after 12 injections and only about one-tenth after 18 injections. The males were more resistant than the females. Five of 12 animals which had received 15–18 injections, and one of seven animals with 12 injections, were completely cured.

The treatment produced a variety of changes in the adult worms, a marked diminution in size which was proportional to the number of injections, the contents of the intestines were reduced and altered, the testes, ovary and yolk glands were reduced in size and later almost completely destroyed, egg formation was interrupted and then ceased, but one to three months after treatment, the worms which survived recovered their normal appearance and functions.

*Foudadin*—The effects of this drug on the worms were, in the main, similar to those produced by tartar emetic, but to a lesser degree.

*Emetine*—With this drug, viable eggs temporarily disappeared from the faeces of some of the treated animals. The worms did not decrease in number in size and the genital organs were unchanged, but the yolk glands reacted by secreting a mass of yolk cells which entered the ovary and caused a clubbed swelling of the uterus, interfering with the functions of these organs. None of the females were unaffected and continued to lay normal eggs. None of the ten animals was cured.

J J C Buckley

RODRÍGUEZ CASTRO, J. Fasciolosis hepática en general, y en especial en España [Infestation by *Fasciola hepatica*, in particular as it occurs in Spain] *Med Colonial* Madrid 1947, Oct 1, v 10, No 4, 221–68, 2 figs & 3 pls [Numerous refs]

The first part of this article need only be mentioned, as the facts related are well known to readers of this *Bulletin*. It deals with a description of *F. hepatica*, its life-history, epidemiology, geographical distribution, intermediate hosts, pathology of infection, treatment and prophylaxis.

The second part, relating to its incidence in Spain, is of more interest and importance from our point of view. It was first reported in sheep by Martín de la Calle in 1890 and in the same year in a workman in Segovia. García Solá's report of a case in 1884 is stated by López-Neyra (in 1933) to have been erroneous, the ova of *Diphyllbothrium* being mistaken for those of *Fasciola hepatica*. Cases are evidently rare. The author mentions one in 1944 in a woman of Almuñécar (the ova were found in the faeces and in the bile), five suspected cases in 1945, of which one was confirmed, another had eosinophilia but no ova were seen in the stools and the use of a duodenal sound was not practicable. In 1946, a third case was proved, a sister of the first in Almuñécar, and soon after one was reported to the author by a doctor who had seen an ovum of *F. hepatica* in the stool of a child suffering from an obstinate diarrhoea. There were evidently others, for the author states that "in 3 years six cases have been seen in Spain." Probably—one might say, certainly—with more thorough examination and more doctors on the look out for cases, the numbers positive would rise, but they cannot as yet be numerous.

differential diagnosis may be perplexing, the author and his colleagues applied the intradermal test with *Dirofilaria immitis* antigen to men who had served in the Pacific.

He discusses the varying results of this test obtained by TALLAFERRO *et al* [this Bulletin 1931 v 28, 214] and SAUNDERS *et al*. (*ibid.* 1947 v 44 108).

In the present case, 200 men were tested at the U.S. Naval Hospital, Aiea, Oahu, between July 1944 and August 1945. A saline extract of *D. immitis* was used, standardized to contain 0.0005 mgm. of protein per cc. The test was made intracutaneously in the forearm with 0.1 cc. of the solution. No control antigen was used. The results were recorded as Immediate (after 15 minutes and 1 hour) and Delayed (after 24 hours) in terms of 1 plus to 4 plus, according as there was, in the former erythema of from 1 to 4 cm., from that with no weal, up to a weal with pseudopods and, in the latter erythema between 1 and 4 cm. with increasing degrees of subcutaneous oedema.

Results of 2 plus or more were called positive. Of 128 patients with a diagnosis of filariasis, 94 (73 per cent.) were positive of 21 who had lived in Samoa, but who had no evidence of filariasis, 6 (29 per cent.) were positive. In the case of 53 patients who had not been in Samoa or Wallis (and therefore presumably had not been exposed) 10 or 19 per cent. were positive.

In the filariasis group of 64 immediate reactors, 13 were negative at the end of 15 minutes, but positive at the end of an hour. 9 of these were also negative after 24 hours, so they would have been missed if no reading had been taken at 1 hour.

The author notes that SAUNDERS *et al.* (*loc. cit.*) had found 81 per cent. of positive reactors among filariasis patients who had been in Samoa, but only 45 per cent. in those who had not. The present series revealed no such difference but among those not diagnosed as having filariasis, the author found 29 per cent. of positives among those exposed in Samoa, compared with 19 per cent. in those who had not been exposed there. Three positive reactors were found among five patients having *Schistosoma japonicum* infections: no positive results were found in four persons suffering from hookworm or in one each suffering from *Acaris Strongyloides* and *E. histolytica*.

The author concludes that while the intradermal test with *D. immitis* antigen is of some diagnostic value for filariasis, it cannot be depended on exclusively as it was negative in 25 per cent. of suspected cases and positive in 19 per cent. of controls.

H J O'D Burke-Gaffney

AGAVRILIOAE, A. Considerațiunile asupra unui caz de *Filaria bancrofti*. [A Case of *Wuchereria bancrofti* Infection (in Rumania)] *Rev. Științelor Med.* Bucharest. 1946, Sept. Dec. v 36 Nos. 9/12, 719-27. French summary (3 lines).

This paper describes the finding of *Mf. bancrofti* in a Rumanian airman in Rumania. It is stated to be the first case reported in that country.

H J O'D Burke-Gaffney

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HARTZ, P. H., HUGENHOLTZ, M. J & VAN DER SAR, A. Helminthiasis Infection of the Wall of the Gallbladder. *Arch. Pathology* 1947 Apr v 43, No. 4 408-11 2 figs. [Refs. in footnotes.]

In the wall of the gall bladder removed from a woman aged 28, a native of Surinam the authors found a necrotic worm in a subserous lymphatic vessel, and eosinophil infiltration. The patient had, some years earlier shown micro-filariae in the blood but schistosomiasis had never been diagnosed. The

worm could not definitely be identified, but it was too large for a larval *Ascaris*, and was probably not a schistosome. The authors think that it was probably a filaria [presumably *Wuchereria*]  
*Charles Wilcocks*

BLOEM, T F, HUYSINGA, J K & WILDERINK, G C [Treatment of Oxyuriasis with Phenothiazine] *Nederl Tijdschr v Geneesk* 1947, July 19, v 91, p 1946 [Summary taken from *J Amer Med Ass* 1947, Nov 8, v 135, No 10, 676]

Bloem and his associates regard phenothiazine as an excellent remedy against oxyuriasis. The patient must be kept under close supervision before, during and after this treatment, and only preparations that have been tested for purity should be used. Hepatic and renal lesions and severe anemia are contraindications to this treatment. As an adjuvant the authors occasionally treated the anal area with a mixture of tumenol, zinc oxide and an anesthetic and prevented constipation. The treatment continues for two consecutive days and is repeated after three weeks. The authors used powders into which 1.25 Gm of phenothiazine had been mixed. Children aged 2 to 4 years were given one powder a day, those 4 to 8 years two powders a day, those 8 to 13 years three powders a day, those 13 to 18 years four powders a day and adults six powders a day. A colorimetric determination of the excreted phenothiazine in the urine is described. One hundred and twenty-three patients were successfully treated. In 1 patient who had been given an overdose of the drug there developed hemolytic anemia.

## DEFICIENCY DISEASES

WOODMAN, H M Nutrition of the African in Tsetse-Fly Areas *East African Med J* 1947, Sept, v 24, No 9, 315-36, 1 pl [35 refs]

No scale of recommended dietary allowances has so far omitted meat and milk. Evidence is presented in this paper that these foods can, at least for the race and environment described, in which cattle cannot be kept because of tsetse, be satisfactorily substituted by non-animal foods, and the resulting diet lead to optimum health and development. The paper is modestly described as a "curtain-raiser" to some field nutrition survey work now being undertaken, though qualitative, the observations, conclusions and recommendations will be found to have value far beyond the southern Sudan.

*Foods*—Meat is only eaten at irregular intervals during a short hunting season. Fish, eggs and milk are rarely if ever used as food. The typical dietary consists of eleusine-manioc flour as a staple, with a wide variety of vegetables, roots, greens and fruit, ground-nuts, beans, oils and other cereals such as maize and rice. (A table of food values of common Sudan foods is given, including some new values.) It might be expected that such a diet would be deficient in high-grade protein, calcium and, seasonally, in vitamin C.

*Nutritional Status*—The Africans of the southern Sudan are of fine physique, strength and stamina and appear to have a high resistance to endemic diseases such as schistosomiasis and ankylostomiasis. The major deficiency diseases are not found. A few conditions attributable to malnutrition, such as xerosis, phrynodema and "mosaic skin" are sometimes but not commonly seen, and three diseases, to the causation of which deficiency is probably contributory, are common—namely tropical ulcer, dental caries and leprosy.

*Improvements in Nutrition*—The author puts forward suggestions for improvement of nutrition as part of a general scheme for raising the standard

of living. The scheme is formulated within the existing framework of social and agricultural customs and food habits. Measures directly concerned with food production include control of shifting cultivation and establishment of families in areas of up to 40 acres each, increased production and improved methods of preserving green vegetables, wider use of the soya bean, the use of food yeast, and the preparation of margarine in areas where vegetable oils are abundant. The author emphasises, however, that these are only details in a development programme which is mainly economic, social and educational.

*Deane A. Smith*

JACQUES J. J. C. Contribution au traitement du "Mbuaki" ou syndrome de dépigmentation du Kwango et du Kasai. [The Treatment of Mbuaki, the Syndrome of Depigmentation, in the Belgian Congo.] *Ann. Soc. Belge de Méd. Trop.* 1947 Mar 31 v 27 No. 1 73-82.

This is the latest of a valuable series of papers from the Belgian Congo on the disease known there as "mbuaki" or "mbuaki". [See VAN DAELE, this *Bulletin* 1939 v 36 913; PIERAKITS *ibid.* 1943 v 40 406; 1947 v 44 225; DOUGER *ibid.* 1947 v 44 431.] It deals mainly with pathogenesis and treatment, the clinical picture having been adequately described by previous authors.

Treatment was directed primarily against the anaemia, which is one of the outstanding features of the disease. The results are summarised in 6 cases, all infants. All were treated with inorganic iron and anthelmintics. One group in addition received intramuscular injections of liver extract, and another—the largest—was given daily intraperitoneal injections of maternal blood, according to the method described by LODGEWYCK [*Rec. T. Serv. Soc. Méd. Congo Belge* 1944 no. 2, 157]. In all three groups there was, in most cases, an increase in the haemoglobin level as measured by the Talqvist method. The author makes the important point that the treatment of these patients in hospital may lead to mistaken conclusions about the result and mode of action of therapeutic measures. It is difficult to separate the effect of hospital diet and régime from that of drugs, and this invalidates the conclusions.

As regards pathogenesis, the author concludes that neither intestinal parasites nor malaria play an essential part in causing the disease, although both may aggravate it. The primary cause is a deficiency of protein and an excess of carbohydrate in the diet. In view of the response to iron, there is probably an iron deficiency but vitaminoses are secondary.

[It is of interest that the workers in the Belgian Congo have reached the same conclusions about the cause of this disease as that derived from a study of similar cases many thousands of miles away in the West Indies (WATERLOW this *Bulletin* 1947 v 44 841; *Medical Research Council Spec. Rep. Ser. No. 263* in the press). In both groups of cases protein lack and carbohydrate excess have appeared to be the main causes, with vitamin deficiencies playing a secondary part. The Belgian writers have laid much stress on anaemia, which is not prominent in the West Indian cases. The latter however do not suffer from either malaria or intestinal parasites. This supports Dr Jacques' view that these conditions are not of primary importance.] *J. C. Waterlow*

PASSMORE R. Mixed Deficiency Diseases in India: a Clinical Description. *Trans. Roy. Soc. Trop. Med. & Hyg.* 1947 Oct., v 41 No. 2, 189-208. [37 refs.]

It has been pointed out by TROWELL [this *Bulletin* 1946, v 43, 1062] that the classical deficiency diseases are rare in Africa, whereas the effects of inadequate food intake are widespread. The same is true of India—beriberi, florid pellagra,

scurvy and rickets are seldom seen, but a symptom complex caused by varying degrees of mixed deficiency of total calories, protein, A and B-complex vitamins, and complicated by protozoal and helminthic infestations is distressingly common

Though brief reference is made in this paper to the probable causation of individual manifestations by individual nutritional deficiencies, it is mainly devoted to a description of the over-all clinical picture seen in the common multiple deficiency state. There may be wide variation among individuals, the effects of one deficiency predominating or one system being mostly affected, but there is discernible in all cases a basic pattern which is substantially the same as that seen in Africa and other parts of the world

**General**—Loss of weight and listlessness are prominent early features. A profound depression and lack of the will to live may prove a serious obstacle in treatment

**The Skin**—Superficial hyperkeratosis with atrophy of the sebaceous and sweat glands produces a skin which is dry, rough and scaly, and which has a crazy pavement appearance. Tropical ulcer is often associated with these changes, but the part played by nutrition in its aetiology is still uncertain. There is frequently involvement of the hair follicles, which gives rise to the distinct and characteristic follicular hyperkeratosis. Angular stomatitis, cheilosis and lesions of all muco-cutaneous junctions are attributed mainly to riboflavin deficiency

**The Eyes**—Xerophthalmia, keratomalacia and Bitot's spots with impaired dark adaptation (mainly avitaminosis A) are probably the commonest signs of malnutrition in India, superficial keratitis and nutritional amblyopia are common only in the south

**The Digestive System**—In most cases of malnutrition, glossitis and diarrhoea are present, the latter being the principal cause of death, general atrophy of the whole intestinal tract is usually seen at post-mortem examinations. Liver function in cases of malnutrition has been little investigated in India, in fatal cases, the liver is usually small and invariably fatty

**The Cardiovascular System**—There is usually evidence of cardiac atrophy with hypotension. Anaemia is usual, with some degree of macrocytosis but the haematological picture is variable and probably represents the combined effects of nutritional deficiency and chronic malaria

**Treatment**—To secure a right psychological attitude and active co-operation is the first essential. This involves a cheerful ward, willing staff, attractive food and a certain pandering to the patients' whims. Milk is the standby in most cases. Vitamin preparations are of use in individual symptom-groups, but rarely achieve complete cure. Yeast products are of value, especially in out-patient work. The necessity for adequate treatment of co-existing infections and infestations is emphasized

Two printing errors have slipped in, their presence in no way diminishes the value of this excellent paper. On page 201 'the value of vitamin A (anurin) therapy' (next paragraph) Vitamin B<sub>1</sub> (thiamine) has been should obviously read 'the value of Vitamin A therapy'. Vitamin B<sub>1</sub> (thiamine or anurin) has been. And the paragraph heading on page 203 'Treatment of Carcinoma Infections' should presumably read 'Treatment of Concurrent Infections'.

Dear A. Smith

BRADY W. R. Malnutrition of the Nervous System. *Brit Med J* 1947, Nov. 15, 703 b, 41, 2nd edn.

It has recently become increasingly apparent, that a number of neurologic diseases are related to defects of diet or defective absorption of essential

nutrients. This relationship was the subject of a discussion at the Neurological Section of the International Congress of Medicine in September 1947 when this was the introductory paper.

As befits an opening paper it deals with the problems in general and slightly provocative terms. It uses as examples chiefly the neuropathies recorded in prison camps during the second world war.

In the main the discussion centres on the question: Intoxication or deficiency? and the difficulty of this apparently simple distinction is well exemplified in the cases of beriberi and arsenical poisoning. In the former which is due basically to a dietary vitamin deficiency the tissues may well be damaged by products of imperfect intermediary metabolism, in fact by local intoxication whereas in the latter it has been shown that arsenite interferes with the pyruvate enzyme system and in arsenical poisoning the damage may be, in effect, due to local enzyme deficiency.

On somewhat parallel lines are discussed the aetiology of pellagra, Wernicke's encephalopathy, painful feet, the captivity cord syndromes and captivity cranial nerve lesions.

Dean A. Smith

NICHOLLS L. Thiamine of Milled Raw and Parboiled Rice. [Correspondence] *Nature*. 1947 Aug 30 298.

It is known that a large part of the thiamin of wheat, rye, maize and barley is in the scutellum of the grain (39 per cent. of all the thiamin of wheat is in the scutellum) and it is probable that the same is true of rice. It has usually been assumed that when rice is parboiled, some of the thiamin is distributed from the germ into the whole grain, and that subsequent milling and removal of the germ does not therefore completely eliminate the thiamin. Nicholls, however, has examined milled parboiled rice grains and compared them with milled raw rice grains and concludes that the effect of parboiling is rather to make the scutellum more adherent so that in subsequent milling only part of it is removed, and therefore part of the thiamin is retained. With raw rice the whole germ is removed. Parboiling may cause some distribution of the thiamin throughout the grain, but its chief effect is probably retention of the scutellum.

Charles Wilcocks

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## SPRUE

BLACK, D. A. H. & SIMPSON, J. A. Serum Lipides in Tropical Sprue. *Tr. Roy Soc. Trop. Med. & Hyg.* 1947 Oct. 41 \ 2, 741-54 [12 refs.]

Estimations of total fatty acid, lipide phosphorus and cholesterol were estimated in the serum of 18 patients suffering from tropical sprue and of 9 normal persons. These were repeated at intervals after a standard meal containing 18 gm. of fat. The fasting level of total fatty acid in sprue did not differ significantly from normal values, but phospholipide and cholesterol were significantly lower. After a fatty meal, the total of fatty acids increased less in sprue patients than in normal persons, but phospholipides showed a smaller increment than did neutral fatty acid. The cholesterol usually fell in sprue patients. No significant change was demonstrated in the fat curve after a period of liver treatment in four patients.

This low fat curve in sprue fits in well with the more direct evidence of faulty fat absorption given by stool analyses. The observed changes can be

well explained on the basis of STANNUS's hypothesis [this *Bulletin*, 1943, v 40, 259] that the absorption defect affects only those lipides which are phosphorylated during absorption, but they cannot be said to prove it

P Manson-Bahr

ELDER, H H A **Clinical Features, Diagnosis, and Treatment of Sprue** *J Trop Med & Hyg* 1947, Nov, v 50, No 11, 212-18

Four hundred cases of sprue were investigated and treated, all were in British soldiers. A table giving the place of origin shows that 75 per cent arose in Bengal, Assam or Burma. This is shown below —

Bengal, Assam and Burma	306
W India	44
S India and Ceylon	27
Central, North, North-West India and Overseas	23

The highest seasonal incidence in India, Assam and Burma was in May, June and July

Long residence is not essential, as the following table suggests —

Residence of 6 months-1 year	37 (9.25 per cent)
„ 1-2 years	147 (36.75 per cent)
„ 2-3 years	171 (42.75 per cent)
„ Over 3 years	45 (11.25 per cent)

Descriptions are given of the various clinical manifestations. For fat analyses, the patients were given, for three days, a diet containing about 23 gm of fat, and a typical specimen of each stool passed during the three days was collected. An analysis was made of the mixture.

In 40 per cent of cases, the total faecal fat was within normal limits, and it was shown that fully established sprue can persist in the absence of steatorrhoea. In a control analysis on the stools of 10 healthy men under the same conditions, the mean total faecal-fat was 29.3 per cent of the dried stool, the maximum being 34.4 per cent. Out of the total —

Glossitis was present in	393
Stomatitis was present in	212
Angular stomatitis was present in	177
Cheilitis was present in	62

The diagnosis and prognosis of the disease are discussed.

In treatment, sulphaguanidine (given in the acute stage) with an initial dose of 7 gm and then 3.5 gm every four hours up to a total of 60 to 70 gm checked the diarrhoea and caused a marked improvement in the general condition. Liver was used in the treatment of anaemia and vitamin preparations for local lesions, with variable results.

Detailed clinical notes of four cases are given. Four diet schedules are set out in an appendix.

P Manson-Bahr

WEIR, J F & COMFORT, M W **Folic Acid Therapy in Nontropical Sprue: Results of Treatment in Seven Cases** *J Lab & Clin Med* 1947, Oct, v 32, No 10, 1231-41

These seven cases have been worked out in great detail, and no useful purpose can be served by summarizing all the data.

Control data were collected before institution of treatment, and special attention was paid to the frequency, duration and severity of the exacerbations, including frequency and character of stools. Haematological studies included

sternal puncture. The concentration of calcium phosphorus, total protein, albumin and globulin in the serum, as well as values for phosphatase and prothrombin times, were determined. X-ray examination of the skull, hands and teeth for osteoporosis, as well as of the small bowel for the so-called deficiency pattern, was secured. In four subjects the faecal solids, fats and nitrogen were determined daily during a three-day test period.

Vitamins, including sufficient vitamin K to control hypoprothrombinaemia, were given. The dosage of folic acid usually was 50 mgm. daily by the intramuscular route.

Treatment with folic acid did not result in improvement in the sense of well-being, gain in weight or strength that could not be equally well accounted for by increased intake of food, and natural remission of the disease. Frequency or severity of exacerbation of the intestinal manifestations did not change. Moreover the haematological response was disappointing. All these points are in marked contrast to the favourable responses of tropical sprue to folic acid. Whether the two conditions are different, or whether these cases had advanced to an irreversible stage is impossible to state. P. Manson-Bair

## HAEMATOLOGY

FINDLAY G. M., BOULTER, E. A. & MACGIBBON C. B. A Note on Sickness and Flying. *J. Roy. Army Med. Corps.* 1947 Sept. v 80 No. 3 138-41

Experiments were carried out in West Africa to determine whether a flight up to 15 000 feet above sea level, without administration of oxygen, would induce an acute haemolytic crisis in Africans with sicklaemia.

Three Africans with sicklaemia showed no ill-effects from such a flight although all showed the presence of sickled red cells at 15 000 feet above sea level after ten to fifteen minutes at this height.

"Differences in the rate at which sickling occurred; were in different individuals were noted and are correlated with the *in vivo* findings."

BENJAMIN PINTO, H., CARBONELL, L., GIL, J. A. & GÓMEZ, O. L. Primera descripción de la anemia drepanocítica en Venezuela. [First Record of Malaria-Called Anemia in Venezuela.] *Rev. Politécnica Caracas.* 1947 Jan. Feb. 16, No. 82, 1-29, 7 figs. [25 refs.]

A very detailed report of case.

## EPIDEMIC DROPSY

MITRA, K. & RAO K. K. P. N. Investigations into an Outbreak of Epidemic Dropsy. *J. Indian Med. Ass.* 1947 June, v 16 No. 9 303-8.

The authors were called upon to investigate a sudden outbreak of bowel complaints associated with swelling of the extremities. [No dates or names of places affected are stated, so the report is deprived of much of its value as a historical record.] Four hundred and fifty-eight persons were affected out of a total of 794 the adults being railway employees. The diagnosis rested between beriberi and epidemic dropsy. None of the patients was under



8 months of age, the percentage of infected rose from 17 (8 out of 47) below two years of age, to 65.7 (136 out of 207) adult females and 75.5 (173 out of 229) adult males. Investigation traced the source to mustard oil purchased at the railway provision store. As some time had elapsed since the start of the outbreak, only nine samples of the mustard oil could be collected. Six of these gave the Argemone oil reaction of LAL and his colleagues. The symptoms were typical. Abdominal pain and discomfort, flatulence, diarrhoea for 3-5 days, occasionally more, followed by swelling of the legs. In a few patients the swelling of legs preceded the diarrhoea. Palpitation and shortness of breath were also complained of. The interval between obtaining the oil and the onset of symptoms ranged between 9.3 and 15.6 days, with an average of 11.3. The outbreak died down rapidly when issue of the oil from the store was stopped.

H Harold Scott

## DERMATOLOGY AND FUNGUS DISEASES

KERVAN, P & ARETAS, R. Deux cas d'histoplasmosis observés au Soudan français [Two Cases of Histoplasmosis seen in the French Sudan] *Bull Soc Path Exot* 1947, v 40, Nos 7/8, 270-76 [11 refs]

[The two cases described in this paper are the same as those noted in this *Bulletin*, 1947, v 44, 1018. These cases, and two cases of histoplasmosis from tropical Africa identified by the reviewer in 1943 and 1946 respectively—the only authentic cases of the disease so far reported from this part of the world—all showed the larger form of *H capsulatum* in the lesions.]

J T Duncan

EMMONS, C W, BELL, J A & OLSON, B J. Naturally occurring Histoplasmosis in *Mus musculus* and *Rattus norvegicus* *Pub Health Rep* Wash 1947, Nov 14, v 62, No 46, 1642-6 [14 refs]

In a previous paper [this *Bulletin*, 1947, v 44, 848], the authors reported the discovery of histoplasmosis in a house mouse (*Mus musculus*) during an investigation on the occurrence of the disease in an area of Loudoun County, Virginia. The present paper deals with the continuation of this investigation and records the discovery of histoplasmosis in 10 wild rats (*Rattus norvegicus*) trapped on three different farms. It is noteworthy that the infected animals showed no macroscopic sign of the infection and they were detected only by cultivation of *Histoplasma capsulatum* from their tissues, chiefly the liver and spleen. Thus, the first recorded discovery of naturally acquired histoplasmosis in wild rodents, constitutes a very important advance in the elucidation of the puzzling epidemiology of the disease, albeit the infection is not known to be transmitted directly from animal host to animal host.

Additional observations were the discovery of *Blastomyces lanuginosa* in one mouse, and a species of *Cryptococcus*, pathogenic for experimental animals, which was isolated from 81 animals, chiefly rats and mice.

J T Duncan

KURZ, E R H & LOUD, N W. Coccioidomycosis in New England *New England J of Med* 1947 Oct. 23 v 237 No 17 610-16 5 figs [21 refs]

A discussion of four cases in returned servicemen

## HEAT STROKE AND ALLIED CONDITIONS

MARRIOTT H. L. Water and Salt Depletion. *Brit. Med. J.* 1947 Feb. 15  
Mar 8 & 15 45-50 285-90 & 328-32, 10 figs. [122 refs.]

(The Croonian Lectures delivered at the Royal College of Physicians, London December 1946)

Water and salt are perhaps the most important substances it is in our power to administer in a wide variety of clinical conditions. They can be so used as to achieve seeming miracles or so misused as to lead to avoidable fatalities. The effects of water and salt depletion have commonly been confused recent experimental and clinical work have made it possible to recognise with certainty the separate effects and to treat them on sound physiological lines.

In the present paper the author presents a lucid and immensely valuable summary of the whole subject.

Among the important physiological considerations vital to the understanding of water and salt depletion are —

- (1) The distribution of body fluid between the intracellular (about 35 litres in an adult man) and extracellular (about 14 litres) compartments.
- (2) The subdivision of the latter into plasma (about 3 litres) and tissue or interstitial fluid (about 11 litres) and the constant to-and-fro filtration which occurs between them, governed by hydrostatic pressure and by the colloid osmotic pressure of the plasma protein.
- (3) The necessity for maintaining osmotic isotonicity of the tissue fluid as the internal environment of cells, distribution of water between cellular and tissue fluids being determined by the osmotic pressure of electrolyte ions.
- (4) Renal regulation of extracellular fluid osmotic pressure by selective reabsorption of components of the glomerular filtrate.
- (5) The magnitude of the daily "unavoidable" loss of water by vaporization (lungs and skin, 1 000 ml.) and as the minimum urine volume for excretion of waste products (500 ml.)

*Pure water depletion* occurs when water intake stops or is greatly diminished and when there is no significant sodium chloride loss in secretions. It may be caused by deprivation of water as in shipwreck, or by inability to swallow as in severe dysphagia, great weakness or coma. The extracellular fluid becomes hypertonic because water is lost without parallel salt loss, water is sucked from the cells, extracellular fluid volume tends to be maintained and dehydration is principally cellular.

*Pure salt depletion* occurs when there are abnormal losses of sodium and chloride in the presence of adequate water intake. It may arise in severe vomiting or diarrhoea from any cause continuous gastro-intestinal suction drainage biliary or intestinal fistulae Addison's disease or most characteristically in heat exhaustion (severe sweating accompanied by free drinking of unsalted fluids). The osmotic pressure of the extracellular fluid falls and the kidneys excrete water to maintain its isotonicity. This leads to diminution of extracellular fluid volume—secondary dehydration. There follows the condition of oligæmic circulatory failure or shock and death is due to decreased blood volume and increased blood viscosity. There may be, as a secondary effect, disturbance of the acid-base balance when there is asymmetrical loss of sodium or chloride ions, e.g. alkalosis in severe vomiting and acidosis in diarrhoea (as in cholera).

The effects of water and salt depletion are compared in the following table —

Manifestation	Pure Water Depletion	Pure Salt Depletion
Dehydration	+++ primary or simple	+++ secondary or extra-cellular
Thirst	+++	Absent
Lassitude	+	+++
Orthostatic fainting	Absent till late	+++
Urine volume	Scanty	Normal till late
NaCl in urine	Often +	Always absent (except in Addison's disease)
Vomiting	Absent	May be +++
Cramps	Absent	May be +++
Plasma NaCl	Slight increase or normal	Greatly decreased
Blood urea	+	+++
Plasma volume	Normal till late	Greatly decreased
Haemoconcentration	Not till late and slight	+++
Blood viscosity	Normal till late	Increased +++
Blood pressure	Normal till late	Fall +++
Water absorption	Rapid	Slow
Mode of death	' due to rise of osmotic pressure	Peripheral circulatory failure

Adequate treatment depends not only upon an accurate qualitative diagnosis, but on an estimate of the quantitative extent of the deficiency in terms of deficit of water or of isotonic saline, either may be as high as 10 litres. In this connexion and in control of treatment the simple and rapid method of FANTUS (*J Amer Med Ass*, 1936, v 107, 14) for estimating chloride in urine is invaluable (details of technique and interpretation are given and may also be found in this *Bulletin*, 1944, v 41, 74)

**Treatment**—In water depletion, water should be given by mouth or per rectum unless circumstances compel parenteral administration, in which case isotonic glucose solution (5 per cent) is the best vehicle for the water. In salt depletion, isotonic saline solution should be used until symptoms are relieved or until chloride reappears in the urine, when it should be replaced by hypotonic ( $\frac{1}{2}$  to  $\frac{1}{3}$  isotonic) saline. The aim should, in either case, be to achieve a minimum urine volume (in an adult) of 1 pint per 8 hours with a salt content of 3 to 5 gm per litre.

An adult suffering from any significant degree of either water or salt depletion will need to receive within the first 24 hours at least a gallon ( $4\frac{1}{2}$  litres) of appropriate fluid

Dean A Smith

## TROPICAL ULCER

GUTCH, C F Local Penicillin Therapy for Tropical Ulcer *U S Nav Med Bull* 1947, Sept-Oct, v 47, No 5, 801-4, 1 fig

The author estimated that about half of the Chinese coolies in a camp in Szechwan Province suffered from tropical ulcer. The hygienic conditions of the coolies were bad, undernourishment was rife, malaria and tuberculosis were common and parasitism was almost invariably present.

The ulcers were readily differentiated and they followed in general the classical descriptions, with spirochaetes, fusiform organisms and secondary

bacteria. The usual lengthy series of treatments were tried with varying degrees of success, but it is noted that local applications of sulphamamide powder produced some measure of success in several cases. Initial therapy consisted of cleansing the affected limb with soap and water irrigation of the ulcer with hydrogen peroxide and saline, and removal of as much necrotic tissue as possible.

Owing to inadequate response of the ulcers to other forms of treatment, local penicillin was applied to some of them after initial cleansing. Dry penicillin sodium (100 000 to 200 000 units) was sprinkled over the surface, which was then covered with gauze impregnated with vaseline. This confined the concentrated solution of penicillin (the penicillin dissolved rapidly in the serum of the wound) to the area having most organisms. The patients were seen daily and further applications of penicillin were made if necessary.

In 32 of 35 ulcers so treated, granulation tissue assumed a healthy appearance and peripheral induration diminished significantly in 24 to 72 hours. When the wound became clean it was kept so with sulphamamide powder and dry dressings. In the three more resistant cases, similar results were achieved after 5 to 8 days treatment with penicillin. Most of the patients experienced a local burning after the application—this disappeared in a few minutes, and was the only ill-effect noted.

Details are given of one case in which satisfactory results with penicillin, followed by sulphamamide were obtained, so that on the 10th day "pinch" grafts could be placed on the granulations. The patient had been working throughout the treatment and continued to do so—despite ambulation, all the grafts took and within three weeks thereafter epithelialization was complete. [See also this *Bulletin* 1948 v 43, 858 and 1947 v 44 748, 935]

H J O'D Burke-Gaffary

## MISCELLANEOUS DISEASES

MACCREARY D & BRICKER, A. G. The Incidence of Intestinal Parasites among Civilians employed at certain Naval Air Bases. *U.S. Nav. Med. Bull.* 1947 Sept.-Oct., v 47 No. 5 928-9.

When Parnaramun Field, Natal, Brazil was being surveyed for anti-malarial purposes in 1943 the authors noted that latrine facilities for the hundreds of native labourers were lacking and that heavy faecal pollution of the neighbouring scrub brush was taking place.

Many stools showed evidence of diarrhoea and a preliminary examination of direct smears from 15 fresh stools produced startling results—nine species of intestinal parasites were found, each sample contained at least one species and one contained no less than six. Seven of the fifteen showed *E. histolytica*. The full results are shown in a table.

Examinations were therefore made of walters and dish washers. Similar stool examinations were made at Pici Field, Fortaleza, some 200 miles to the north of Natal, and at Aratu seaplane base and Ipitanga Field, both within 25 miles of Bahia and approximately 30 miles apart, and some 450 miles to the south of Natal.

A total of 133 examinations are recorded from Natal (61) Fortaleza (44) Aratu (15) and Ipitanga (13).

Although only one stool was obtained from each person and no concentration methods were used, not one parasite-free sample was obtained.

Among other findings revealed in a table are that hookworm had the highest incidence, accounting for 71 per cent for the whole group (although Aratu seaplane base produced 93 per cent of *Ascaris*) *Ascaris* accounted for 62 per cent for the whole group *E. histolytica* varied from none at Ipitanga to 27 per cent at Fortaleza and *E. coli* averaged 37 per cent. *Strongyloides* occurred in 13 per cent and the other common parasites in lesser degree.

*Schistosoma mansoni* was found once at Fortaleza, twice at Aratu and three times at Ipitanga it was not found at Natal, where conditions appear to be unfavourable for *Planorbis*.

The authors note the difficulties in avoiding the ingestion of parasites in such an area and the need for rigid precautions to avoid contamination of food and water. Despite the small series, the investigation does represent a segment of conditions in four areas extending some 850 miles along the coast. Although unusual care was taken, one of the authors acquired *E. histolytica* and *Ascaris* infections it is observed that long intervals without fresh vegetables will cause a normally cautious person to "take a chance" H J O'D Burke-Gaffney

DAVIES, J N P Pathology of Central African Natives Mulago Hospital Post Mortem Studies Series III *East African Med J* 1947, Aug, v 24, No 8, 289-303 [26 refs]

Lobar pneumonia has long been recognized as accounting for a high proportion of deaths amongst Africans. VINT, in Nairobi, [*East African Med J*, 1928, v 5, 383] found it responsible for death in 42 per cent of post mortems he performed in one year, and in 1937 [*ibid*, v 13, 332] reported finding the disease in 29.8 per cent of 1,000 consecutive autopsies, the right lung being predominately affected. GARNHAM and DE SMIDT [*ibid*, 1931, v 8, 150], typing pneumococci from 100 cases in Africans, found Type IV in 91 per cent, ORMISTON in England (1942) found this type in England in 61 per cent.

In 2,994 autopsies performed at Mulago, Uganda, lobar pneumonia was found in 15.7 per cent, more persons dying from this condition than any other. Bacteriological examination of 170 cases showed pneumococci in 90 per cent, but right lung involvement was not nearly so marked as in Nairobi. There is no evidence that the disease is more severe than in England, possibly it is even milder. Most of the deaths appear to have occurred in the third decade of life.

Of the 472 cases recorded 37 per cent showed complications due to the infection (*cf* VINT, 1937 *loc cit*, who reported 26.2 per cent in Nairobi). These were as follows —

Group 1	Local complications in the lungs	43 cases (9.1 per cent)
I	Suppurative softening (small abscesses)	3 cases (0.6 per cent)
II	Abscess	33 cases (6.9 per cent)
III	Gangrene of lung (all lower lobe)	8 cases (1.7 per cent)
IV	Delayed resolution and carnification	15 cases (3.1 per cent)

Group 2 Direct spread from lung

Only one case of subphrenic abscess and one of suppurative mediastinitis were noted. Empyemata were found in 43 instances (9.1 per cent) and of 14 cases examined bacteriologically, pneumococci were found in 13, staphylococci in one. Pericarditis occurred in 39 (8.1 per cent), 23 being purulent, there was no evidence that this was usually associated with right lung involvement. In only 2 per cent of the empyema cases were there septicaemic complications.

Group 3 Septicaemic complications

Meningitis 16 (3.3 per cent), 12 of 13 cases were pneumococcal and 1 meningococcal.

Endocarditis 15 (31 per cent.) 9 out of 10 cases examined being pneumococcal and 1 due to *Haemophilus influenzae*. Septicaemic signs without localization were found in 4 cases. One interesting complication was pneumococcal encephalitis—recognized in 12 cases. At autopsy lobar pneumonia was found, the meninges being slightly hyperaemic but without exudate and with sterile cultures—the brain was hyperaemic and in some cases large punctate haemorrhages were found. Portions of the brain removed and injected intracerebrally into animals failed to show a virus but the animals died of pneumococcal meningitis. Peritonitis was found in 6 cases.

The above figures are analysed and compared with those of Oiler & Macrae, and Vint in a table in the text.

Of 253 cases of broncho-pneumonia 40 were apparently primary 26 secondary to enteric fever 35 showed marked malnutrition 40 had syphilis and 29 tuberculous 22 cases occurred in children. Malnutrition and gross structural changes e.g. cirrhosis of the liver are considered to play an important predisposing part in pneumonia, the so-called "tropical diseases" a relatively unimportant one.

The question whether pyogenic infections are more common in Africans than in Europeans requires further surveys but some differences are apparent. Firstly streptococcal infections in Africans are relatively rare and harmless (at any rate in Kampala) this is not the case in Europeans (the reviewer has found the Masi living mostly on blood milk and meat to have a high apparent degree of immunity to this infection.) The pneumococcus shows a greater tendency in Africans to cause septicaemia without lung involvement.

What evidence there is available suggests that the incidence of lobar pneumonia is high in Africans but here it must be remembered that the records come mostly from people herded together in towns industrial areas etc., i.e. away from their normal environment and that the disease is most common in newcomers. The probability is that in his normal habitat the African acquires immunity only to those types common in his district. The theory that blockage of the reticulo-endothelial system is responsible for the frequency of septicaemia is hard to accept and it is difficult to see what infections are to blame—the spleen of many Africans is fibrosed (because of malaria) but much of the reticulo-endothelial tissue lies outside this organ.

It is thought that increased susceptibility to septicaemic and pyogenic disease lies mainly in two causes.

(1) Malnutrition (very common) (2) Poor economic conditions, & severe labour. Liability to constant abrasions and ulcerations of the skin poor housing, exposure to cold and wet all give more opportunity to infection than in Europeans.

[It is a truism to say that more than half the problem of improving the general health of the African lies in better feeding especially with proteins of high biological value.] [For Parts I and II of this series see this Bulletin 1947 v 44 1098.] C. F. Sheldon

## PROTOZOOLOGY GENERAL

SPENA, A. Contributo allo studio della toxoplasmosi e considerazioni sulle diverse specie che costituiscono il genere *Toxoplasma*. [Species of *Toxoplasma*.] *Riv di Parasit.* Rome. 1947 June Sept. v 8, Nos. 2/3, 85-104 6 figs. [19 refs.] English summary (3 lines).

Toxoplasmosis was observed in laboratory guinea-pigs in Addis Ababa. The infection was inoculable from guinea-pig to guinea-pig, as also to the rabbit and

a calf The parasites occurred in all the organs The author discusses the identity of the parasite in relation to *Toroplasma caviae* Carini and Mighano, 1916, and concludes that it is better to consider that a single species exists which would be *T gondii* Nicolle and Manceaux, 1919 C M Wenyon

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## ENTOMOLOGY AND INSECTICIDES GENERAL

KAHN, M C Females Mosquito "Calls" and their possible Significance in Control Kuba Habana 1947, May, v 3, No 5, 119-20

In this short article the author describes how he made recordings of the sounds produced by the females of the following mosquitoes *Anopheles quadrimaculatus*, *Aedes aegypti*, *Aedes albopictus* and *Culex pipiens* The records were made in a sound-proof chamber kept at atmospheric conditions comparable with those in the natural environments of the insects He states that "most of the significant sounds are made while the insects are at rest" and are in the range of from 200 to 8,000 cycles per second The recordings are not audible to the human ear, they "require to be amplified some one-hundred million times or more" He claims, however, that an experienced observer can distinguish the sounds of one genus or species from another and can also distinguish the sounds made by the sexes of the same species When a record of a female voice is played, males of the same species fly towards it, the author therefore hopes to transfer the sounds to magnetic tape for continuous playing and to test its ability to lure males to an electrical device which will kill them [See also this *Bulletin*, 1945, v 42, 661] H S Leeson

GRENIER P Facteurs écologiques conditionnant la répartition des larves de *Simulium* (Dipt) Variations morphologiques spécifiques en rapport avec la vitesse du courant. [Ecological Factors affecting the Distribution of *Simulium* Larvae Specific Morphological Changes related to Rate of Flow of Water] C R Acad Sci 1947 Nov 10, v 225 No 19 901-3, 1 fig

MOOSER H Das synthetische Insektenmittel DDT [The Synthetic Insecticide DDT] Wien klin Woch 1947 Nov 28 v 59 No 47 773-7 [14 refs]  
A general review

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## REPORTS, SURVEYS AND MISCELLANEOUS PAPERS

BARRETT, R H Health Regulations for Air Travel Brit Med J 1947, Nov 8, 741-3 [Summary appears also in *Bulletin of Hygiene*]

The rapidity of air transport at the present time has greatly increased the difficulties of health authorities throughout the world in view of the lack of clinical signs of infectious disease to be expected among the passengers examined It is necessary therefore, to place more reliance on immunization, and hence it is insisted that vaccines of known efficiency should be used and that the passenger should produce proof, in the form of certificates, that the operation has been performed satisfactorily

The author has discussed briefly the methods of control and the regulations in force against the five major epidemic diseases, yellow fever, smallpox, cholera, plague and typhus

In Table I are listed the accepted incubation periods of these diseases, and the periods of validity of the certificates of immunization agreed on internationally

TABLE I

Disease	Incubation Periods	Periods of Validity of Certificates of Immunization
Yellow fever	6 (India) 9 days	For 10 days to 4 years from date of inoculation
Smallpox	14 days	For 14 days to 3 years from date of vaccination
Cholera	5 days	For 6 days to 6 months from date of inoculation
Plague	6 days	Not stated, but usually for 6 months from date of inoculation
Typhus	12 days	For 1 year from date of completion of course of inoculations

*Inoculation and Vaccination.*—The number of inoculations or vaccinations required by a particular passenger depends on the route on which he will fly. It will be necessary for him to comply with the regulations of each country in which he lands as well as those of the country of departure and of his destination. The regulations however usually make a distinction for a passenger who is only in transit through a country and not disembarking into it, and in the former case an abatement of the rules is sometimes permitted. Health authorities are naturally anxious to prevent the entry of a person incubating any disease into a country where conditions are particularly favourable for its spread. This is the case in India, where regulations against the importation of yellow fever are very stringent in consequence of the presence of *Aedes* mosquitoes. Similarly, in Australia, special precautions against smallpox are insisted on.

*Variation in Validity of Immunization Certificates.*—The periods of validity of certificates of inoculation and vaccination as shown in Table II vary in certain countries and it is necessary to ensure that each passenger is in possession of certificates that are valid for all countries in which he will land during his journey. It would, of course, simplify the procedure for passengers if all countries would agree to accept the same periods of validity.

TABLE II

Disease	Convention Validity	Limits & Variation	
		Maximum	Minimum
Yellow fever	10 days/4 years	15 days/2-4 years (India)	15 days/2 years (Madagascar)
Smallpox	14 days/3 years	21 days/3 years (Egypt)	12 days/1 year (Thailand)
Cholera	6 days/6 months	14 days/6 months (Abyssinia)	6 days/3 months (Hong Kong)
Plague	None stated	5 days/3 years (Cyprus)	6 days/3 months (Hong Kong)
Typhus	—/1 year	12 days/1 year (Lebanon)	8 days/6 months (Cyprus)
Typhoid	None stated	6 days/1 year (Borneo)	6 days/3 months (U.S.)

\*Calculated from date of completion of inoculation or of vaccination.

It is important that the passenger and practitioner should take into account the interval of time that must elapse before the certificates of these operations become valid. These periods are referred to in Tables I and II. The



consequences to a passenger who is not in possession of the requisite certificates may be a refusal of permission to embark, an enforced period of quarantine at the port of disembarkation, or refusal of permission to land

In general, vaccination against smallpox and inoculation against the typhoid group should be recommended to any person proceeding abroad Other inoculations need be advised only when epidemics are known to be in progress

If the methods employed to control the entry of disease into countries by air appear to assume an importance not hitherto known in sea or land transport, it should be remembered that practically all international flights are, from the point of view of quarantine, well within the incubation period of the major epidemic diseases

All materials for these inoculations, except yellow fever vaccine, are available for use by practitioners The yellow fever vaccine must be kept under more exact conditions and so is only available for inoculation in certain centres which are listed

A brief description of health regulations affecting aircraft and crew is also given  
*F O MacCallum*

**WORTHINGTON, E B** *A Development Plan for Uganda* With a Foreword by His Excellency the Governor of Uganda, Sir J Hathorn HALL pp xii+112, 10 figs (8 maps) 1946 Dec Entebbe Govt Press [Shs 2/50]

At the present time there is a strong movement to develop the economic and social life of the countries of Africa, and a growing realization that if this is not undertaken thoroughly, and soon, the people will shortly be faced with famine because their agricultural habits are not adequate to keep pace with a rapidly increasing population At the same time there is the realization that although much is known about the economic potentialities of these countries, much remains to be discovered before any rational plan of progress is possible The present volume is the outcome of a study of the problems inherent in any scheme of development Dr Worthington's wide knowledge and experience have enabled him to correlate the different sides of the subject, and to formulate proposals

He discusses the matter under various headings —The fundamental problem, finance, the productive services, social services, the common services, and special developments The chief and most stubborn fact of the fundamental problem is that the present population of about 4,000,000 is likely to increase to 10,000,000 in the next 50 years, and that the productive capacity of the soil will then be used to its fullest extent, if all suitable land is made available At present the land is not all available, but much more could be worked if, for instance, lack of water was made good The country could support this enlarged population if the output per person were increased, and if the large areas now unused were rendered usable

This plan cannot satisfactorily be summarized, and readers are referred to the original for details of the many enquiries made and opinions expressed The author has received much assistance from those who have worked in Uganda, and studied its problems, for many years  
*Charles Wilcocks*

**KALRA, S L** *Addu Atoll (Maldivé Islands) Its People and Its Important Diseases* *J Indian Army Med Corps* 1947, July, v 3, No 3, 137-41

The Maldivé Islands are atolls, rising no more than a few feet above sea level, the soil is mainly soft coral sand, rich in lime Vegetation is abundant, and palms, plantains, breadfruit, papayas, sweet potatoes and other bulbous roots grow prolifically, the growth of scrub is very thick Swamps, some of sweet water, abound, and fresh water is easily obtained from shallow wells The

average rainfall is 68 inches per annum. The author describes the conditions of life which have already been recorded by MARSON (this Bulletin, 1943, v. 43, 1202).

The common diseases are scrub typhus, malaria, filariasis and dysentery. The only *Anopheles* is *A. tessellatus* which breeds solely in wells of fresh water. It has been found infested in nature. The range of flight of *A. tessellatus* is more than half a mile but less than two miles. In wells containing small fish (*Barbus* spp.) no mosquito larvae could be found. Spleen rates are fairly high. Culicine mosquitoes are abundant.

Scrub typhus is probably carried by *Trombicula delausis* in these islands; the local people are apparently immune and cases have been found only in the garrison. Filariasis is due to *Wuchereria bancrofti* and both *Culex fatigans* and *C. sinensis* have been found infected. Filariasis is present in all villages.

Ulcers of the legs, due to secondary infection of injuries from coral, are fairly common.

Charles Wilcocks

PEARCE, A. S. [Edited by]. *Zoological Names. A List of Phyla, Classes, and Orders.* Prepared for Section F American Association for the Advancement of Science. 22 pp. 1947. Durham, North Carolina.

A second edition of this list which was first issued in 1936 and which has been out of print for several years, has now been published. In this, a number of corrections have been made. The list does not go beyond suborders.

In his preface to the first edition the editor discusses some of the difficulties attending any effort to achieve uniformity in zoological nomenclature, and admits that he has been unable to do so. He names the large number of experts who have advised him on the nomenclature adopted in the various sections. Two columns are given on each page the first comprising the names (with authors and dates) which the editor after consultation believes to be in best current usage the second containing the names which a few zoologists would like to see used. The following endings are adopted—Phylum and Subphylum, -a Class, -ea Subclass, -ia Order, -ida Suborder, -ina.

This is a most useful reference list, which will help zoological teachers and students (including medical men interested in tropical diseases) to avoid some of the confusion which now exists in zoological nomenclature.

Charles Wilcocks

## BOOK REVIEW

BLACKIE W. A. (M.D., Ph.D. F.R.C.P. (Ed.) D.T.M. & H. Hon. Consulting Physician, Salisbury Hospital, Southern Rhodesia, etc.) *Malaria, with special reference to the African Form.* 101 pp. 44 coloured figs. on 1 pl. 1947. Cape Town. Published for the Post-Graduate Press by the African Bookman. [10s. 6d.]

This monograph on malaria is the first book to be published for the Post Graduate Press of Cape Town with the aid of a grant from Messrs. Bayer Pharma Ltd. It is written from the point of view of the general practitioner and specially for those working in Africa. It is for the latter reason that the book has a particular value. None of the standard text-books on tropical medicine, nor the earlier monographs on malaria, gives quite such a clear

picture of those forms of the disease encountered in tropical and Southern Africa. No one has yet demonstrated the exact nature of the differences that exist between African and classical malaria and the author makes no claim to have done so, though he takes the generally accepted view that strains of parasites and the degree of immunity in the indigenous population are important factors. He also points out that the high order of premunity prevailing among the adult population calls for a very different approach to the diagnosis of any acute fever.

The book comprises a clear account of the parasitology and pathology of malaria, the clinical features and treatment. It is confined to human forms of the disease, and it does not include within its scope a description of the anopheline vectors, epidemiology, or of measures of control. There is a coloured plate which gives an adequate picture of the various species of malarial parasites, though it omits the degree of magnification and the method of staining, and it includes *Plasmodium tenue*, a parasite which is not mentioned in the text.

The author adopts the unusual clinical classification into the following forms —

#### *In Europeans*

- 1 Acute benign malaria—due to *P vivax*, *P ovale* or *P malariae*
- 2 Acute malignant malaria—due to *P falciparum*
- 3 Chronic malaria

#### *In Africans*

- 1 Acute malaria—due to any species
- 2 Chronic malaria

This classification may be of value to the practitioner, but it leads to some overlapping in the description of the clinical features, and its use must tend to the ignoring of species diagnosis which is the only rational approach. A more serious defect is the division into European and African forms of the disease—the division should be into susceptible races and relatively non-susceptible races. Many Africans (i.e., adult Africans) come into the former category and their disease syndromes are identical with those of Europeans. A proper understanding of this problem can only be reached after prolonged study of the nature of immunity and thus, unfortunately is dealt with very sketchily. A book which is written with special reference to the African forms surely deserves more than a page and a half on this subject.

A full account is given of the clinical features and of the different pernicious forms of *P falciparum* malaria. Blackwater fever is not included in this monograph. Some of the statements which echo from text-book to text-book are again repeated here, their accuracy is doubtful and their importance is magnified. To begin with, this emphasis on the protean manifestations of the disease is very little justified. Ross [above, p 141] has recently pointed out the dangerous error of regarding malaria in this way, in the vast majority of cases it is a simple illness easily recognized, and diagnosed for certain by finding parasites in the blood. Again, how valid are all these different forms of pernicious malaria: algid, hemiplegic, bulbar, hyperpyrexial, gastric dysenteric, pneumonic, sudoral etc? How often are these in reality meningococcal meningitis, a virus encephalitis, a bacillary dysentery, heat stroke etc? Lastly may be mentioned the statement that is so often read and for which there is so little evidence, that the infant mortality from malaria amongst African children is heavy. As Sir Leonard Rogers (*Fevers in the Tropics*) has pointed out, when such deaths are more closely investigated, the true figure gets lower and lower (e.g., from 90 per cent to 20 per cent).

In the chapter on diagnosis, the author recommends the use of Giemsa's stain and of Field's rapid method. It is an advantage to become complete master of one or two methods—nevertheless a description of Leishman's stain might have been added, and the J.S.B. rapid stain (this *Bulletin* 1944 v 41: 822) is superior in many ways to Field's. It is strange to find sternal puncture included in aids to diagnosis whilst the much more useful—and therapeutically valuable—method of adrenaline provocation (of Ascoli) is omitted.

In regard to treatment both curative and prophylactic, the author recommends the current standard procedures. He takes a commonsensical view on the use of injections. If the patient cannot absorb the drug by the oral route, then parenteral administration is necessary. In one place, the author gives the curative dosage of mepacrine as 0.3 gm. a day (p. 81) in another 0.3 gm. thrice daily (p. 83) apparently he means the former. All the dosages recommended are perhaps slightly on the high side (e.g. quinine 30 grains daily for approximately 5 days, followed by 0.3 gm. mepacrine daily for 5 days). Not many patients would consent to stay in bed for 3 or 4 days after the temperature has become normal. The author follows the lead of Marchiafava and other Italian physicians in stressing the importance of lumbar puncture in the therapeutics of cerebral malaria.

The danger of becoming over-enthusiastic in regard to a new form of treatment is well illustrated in this book, in the case of paludrine. Fortunately the author had time to insert an addendum, stating that this drug fails to bring about the rapid control of African fever as claimed in the original publications and that severe attacks of malignant malaria have occurred in spite of systematic paludrine prophylaxis.

The book as a whole is full of interest, is well presented and contains few mistakes. The above criticisms of the reviewer are largely on matters of opinion on a subject which is so prone to dogmatism. Genuine mistakes do occur—for instance—the statement that the various members of the genus (*Plasmodia*) "develop in the female anopheline mosquito—instead of in various genera of mosquitoes. Matters of opinion are illustrated by assertions such as hepatic tenderness is almost invariably present (p. 40) in acute malaria. This is perhaps true in Southern Rhodesia where the author works, but it may not be so in other parts of Africa. The statement that wherever Europeans live in an area of endemic malaria it is clearly necessary to supplement all other prophylactic procedures by means of chemoprophylaxis" would probably now be accepted by only a minority of tropical workers.

P. C. C. Graham

# TROPICAL DISEASES BULLETIN

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## SUMMARY OF RECENT ABSTRACTS\*

### III MALARIA .

#### *Epidemiology*

STEVENS and BLACKMAN (p 169) report malaria in two persons, living in Oxford, who had never been out of Britain, and LEVICK and MACGREGOR (p 789) refer to two cases of malaria in London children, which were probably contracted in Welling and the Isle of Sheppey respectively. FERMONT (p 874) also records a case of malaria in a patient who had no previous history of malaria and who had lived for some years in England, but she had lived in the tropics until 1937.

VOGT (p 172) reports a case of malaria apparently contracted in Norway, in which the incubation period was probably 8-9 months. HERNBERG (p 951) states that *P. vivax* malaria, which had been almost absent from Finland for 20 years, was found in Finnish troops during the recent war, and in civilians. The source was, apparently, the Russian troops, and most cases were related to Karelia. In many cases the incubation period lasted 9 months. The same author (p 15) discusses the long incubation period (which may be up to one year) observed in the malaria of Finland, basing his opinions on findings during an epidemic in troops in 1944-45.

Indigenous malaria in Vienna has apparently increased in recent years. WENGER (p 951) attributes this largely to the number of infected persons who have returned from war service.

PUTNAM and HACKETT (p 15) report on malaria in Sardinia during 1925-34, where *A. maculipennis labranchiae* and *A. sacharovi* are the vectors. The density of anophelines and the prevalence of malaria declined sharply in one area after limited control measures had been instituted in 1925.

ALOSI (p 155) shows that during the war there was a marked increase of malaria in Sicily, partly because the people were dispersed as a result of bombardment, and partly because new strains of parasites were introduced by the troops.

KOUSSITASSEFF (p 638) describes the declining incidence of malaria in Bulgaria, where *A. maculipennis*, *A. superpictus* and *A. sacharovi* are the vectors. He ascribes the decline to the antimalaria measures taken, but does not give details.

\* The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin* 1947 v 44. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

BERLEMSCHIEV (p. 630) discusses in detail the possible effects of large-scale migrations of population or of troops, in relation to malaria, and considers these possibilities in the light of actual happenings in Russia during the war. The abstract should be read in full.

SANJUAN FUENTES (p. 486) discusses malaria in the Tangier Zone, where *P. vivax* is the predominant parasite.

WILSON (p. 952) sums up the malaria experience of the troops in Madagascar where *P. falciparum* is the common parasite. Malaria is hyperendemic in parts with high spleen and parasite rates in children. *A. gambiae* is present throughout the island, and is a serious vector but *A. funestus* is the chief carrier in the higher country.

TURNER and WALTON (p. 640) have compiled a detailed report on malaria in Freetown, where the chief vectors are *A. gambiae* and *A. mides*. Transmission is perennial, with great exacerbation during the rainy season, and mosquitoes are often blown out to ships in harbour even as far as two miles from the shore. Although the general sanitary level of the town is low the malaria position has improved since the beginning of the century and during the war the various precautions taken in military units reduced the risk from a probable rate of 1,000 per 1,000 to 73 per 1,000 per annum. At the present time, *P. falciparum* is the predominant parasite.

SCHWITZ (p. 786) finds that the limit of altitude for endemic malaria in the Belgian Congo is about 1 750 metres above sea level.

MATILLA *et al.* (p. 279) report on the spleen rates found in the island of Fernando Po.

COVELL (p. 797) discusses the whole question of the effect of irrigation on malaria in India. The most dangerous form of irrigation is by perennial canal, and the chief sources of danger arise from general raising of the subsoil water level, seepages and leakages. The solution of this serious problem lies in cooperation between the engineer and the malariologist. RAO and NAMUNDOON (p. 16) show how the construction of a dam across a river in Mysore, and of a canal fed from the reservoir thus formed, raised the level of subsoil water practically to ground level, and created conditions in which *A. culicifacies* bred and caused an epidemic of malaria in an area previously fairly healthy which was followed by conditions of hyperendemicity. An enormous multiplication of snails also took place with the result that fluke disease of sheep and cattle caused great loss. In part of Madras a large irrigation scheme is proposed, which involves construction of a large dam, and a large lake. In a preliminary survey of the area, RAO *et al.* (p. 952) found endemic malaria in only 68 of 312 villages, but epidemics occur after seasons of abnormal rainfall. *A. culicifacies* is the chief vector but *A. stephensi* also plays a part.

DE BURCA (p. 953) gives an account of malaria at Fort Sandeman in the north-east of Baluchistan, where *A. culicifacies* and *A. stephensi* are the commonest anophelines. There is evidence that these were caught 3-3½ miles from their breeding places.

HARPER and his colleagues (p. 953) have written a series of comprehensive papers on malaria in the U.S. forces in the South Pacific, where it caused casualties five times as numerous as those due to combat. In the most severe epidemics the incidence was at rates up to 2,678 per 1,000 per annum, but mosquito control and suppression by drugs greatly reduced the incidence. The authors think that *A. farauti* (which they regard as a species rather than a variety of *A. punctulatus*) is probably the only important vector in the South Pacific area—most of the other anophelines even *A. punctulatus*, are zoophilic in habit. MACKERRAS and ARERBERG (p. 535) report a malaria survey at Wewak, New Guinea. The vector is *A. punctulatus farauti* and transmission is probably perennial. Spleen rates and parasite rates and counts are high.

in infancy, and fall in childhood, as does the gametocyte count. The picture is one of hyperendemicity with development of immunity. It is likely that infants provide the sole source of infection of anophelines with *P. falciparum*, since the gametocyte counts in older children and adults are probably too low for effective transmission.

WATSON and RICE (p 35) show that in the Tennessee Valley, negroes suffered less illness from malaria than white persons, but blood examination showed that they had a greater relative number of infections. The negroes lived under similar, or worse, conditions than the white people.

MONTESTRUC (p 641) reports on malaria (largely due to *P. falciparum*) in Martinique, where it is found only on the south coast, and where the incidence is not heavy. BELLERIVE and DAMBREVILLE (p 16) discuss malaria in Haiti, where it is an important problem.

BATISTA (p 875) records malaria (chiefly due to *P. vivax*) as he saw it at a hospital in Amazonas, Brazil.

### *Aetiology*

In a discussion of the generally accepted nomenclature of the malaria parasites of man, CHRISTOPHERS (p 158) argues that although these names are incorrect, according to the rules of nomenclature, to alter them would lead to such confusion that the rules should, in this connexion, be suspended. SABROSKY (p 556) makes a contribution to the question of nomenclature of malaria parasites, which should be read in the original.

In *Federation Proceedings* (p 400) there is a series of papers on the biochemistry of malaria parasites, in which much of the work done in recent years is summed up. This cannot successfully be condensed.

DAVEY (p 954) discusses the question of exoerythrocytic schizogony in human malaria, the evidence that it takes place is indirect, but strong. LANZA (p 160), however, thinks that no satisfactory evidence has yet been found of exoerythrocytic forms of malaria parasites in man, and discusses the various appearances of cells and parasites which are likely to be mistaken for these forms. OBERLÉ (p 159) describes what he considers to be exoerythrocytic forms of *P. vivax* in man, after infection by inoculation of infective blood in 5 patients with general paralysis. In comment, WENYON refers to the fact that merozoites are extra-cellular, and contain no pigment, for part of their cycle, but that they may be taken up by phagocytes and may even undergo some development in them before being destroyed.

FONSECA *et al* (p 487) have studied the infection of chick embryos with *P. gallinaceum*, and the formation of exoerythrocytic stages of the parasite. They have also examined bone-marrow and blood in human infections with *P. vivax* and *P. falciparum*, and they think that there is a reticulo-endothelial phase, preceding the erythrocytic phase, in human as in avian malaria, though they admit that complete proof has not been found. In comment, WENYON gives the opinion that some of the forms described by these authors may be merozoites from erythrocytic schizogony rather than true exoerythrocytic forms.

DUBIN (p 955) describes bodies which suggested exoerythrocytic forms of *P. vivax* in tissue cultures.

DEANE (p 17) shows that the chromatin of *P. vivax* and *P. knowlesi* stains well by the Feulgen technique provided that the slide has previously been exposed to alkaline alcohol, she discusses the reason for this.

SHUTE (p 18) describes the Madagascar strain of *P. vivax* maintained for 22 years in the Horton hospital, and transmitted since 1933 by a strain of *A. maculipennis* raised from a single female.

FERREBEE and GEIMAN (p 17) have devised a centrifugation method for separating infected from non-infected red blood cells, this depends on mixing

together equal volumes of heparinized infected blood and albumin solution of specific gravity 1071

FERRAZZINI *et al.* (p. 17) have conducted a study by injecting radio-active iron, from which they conclude that *P. vivax* tends to invade young red blood cells. BELTRÁN and SANDOVAL (p. 160) show that merozoites of *P. vivax* exhibit a preference for reticulocytes.

BLACK (p. 18) has cultivated *P. falciparum* and *P. vivax* *in vitro* and notes that they grow as well in serum from a malaria patient as in normal serum. He describes the stages observed, noting that cells invaded by *P. falciparum* tend to clump and adhere to any leucocytes present, and that *P. vivax* prefers young red blood cells.

MOSEMOVSKI (p. 956) shows that there is a linear relationship for *P. vivax* and *P. falciparum* between temperature and rate of development in the mosquito. The threshold for development of the latter is higher than that of *P. vivax*.

SMOLINSKAJA (p. 875) found *P. falciparum* in various stages of schizogony in venous blood when finger blood, and sternal and spleen puncture material, contained only ring forms. He thinks, therefore, that the peripheral regions of the venous system might represent the normal sites of schizogony of *P. falciparum*.

SOVIEV (p. 875) has found that the strain of *P. ovale* originally isolated in the Soviet Union, has retained its characteristics during many years of use in the treatment of general paralysis. LISOVA *et al.* (p. 876) have infected various anophelines with this strain but an editorial comment relating to their work suggests that it may not be true *P. ovale*.

BASU (p. 1030) shows the frequency of distribution of gametocytes of the three common species, in a series of gametocyte carriers in India.

#### T. TRANSMISSION

Investigating the entry of hungry *A. maculipennis streptus* into human or animal houses, VAN TRIEL and WEUKMAN (p. 657) conclude that atmospheric conditions are much less important than the odour of pig or man, in attracting the mosquitoes. They (p. 787) have found experimental evidence to indicate that *A. maculipennis streptus* is attracted by CO<sub>2</sub> in the atmosphere up to a concentration of 10 per cent.

ETHERINGTON *et al.* (p. 163) quote evidence which indicates that *A. kyzassus* and *A. maculipennis mesasiatica* usually considered to be of no malaria importance in Italy do in fact transmit in part of the Po valley. It seems probable that these mosquitoes picked up infection from patients with general paralysis treated by malaria therapy in a hospital in which mosquito screening had fallen into disrepair.

ULITCHOVA (p. 162) shows that in Uzbekistan the breeding of anophelines takes place chiefly in swamps during spring and chiefly in rice-fields during summer. PLITNEV (p. 957) names the anophelines found in southern Kazakhstan where malaria is common and VELTISHCHEV (p. 957) those found near Kazalinsk in the same area. Breeding places are described by both these authors. IVANOVA (p. 483) points out that anopheline larvae are capable of crawling over moist surfaces when escaping from a drying pool in search of water. He has studied their reactions to light under these circumstances. USTIKOV (p. 491) has studied the gonotrophic cycles of *A. maculipennis* in the Caucasus—details should be sought in the original abstract.

UNGUREANU (p. 557) describes certain morphological features of females of *A. maculipennis* which greatly assist in the differentiation of adults of the various races. AKALIN (p. 163) reports morphological anomalies in male genitalia of *A. maculipennis*.



ETHERINGTON and SELICK (p 19) record their observations on *A. sacharovi* in Persia and Iraq, where it is commonly associated with spleen rates between 60 and 100 per cent. *A. superpictus* and *A. maculipennis maculipennis* are also found.

USTINOV (p 490) points out that *A. claviger (bifurcatus)* is the commonest mosquito on the Black Sea coast of the Caucasus, and that its larvae develop through the winter, reaching stage IV by March.

KRIVONOSOVA (p 161) and IVANOVA (p 161) discuss the breeding of *A. plumbeus* in tree-holes.

In a comprehensive report, TREDRE (p 488) describes the breeding habits of *A. melas* in the *Paspalum* grass and *Avicennia* mangrove areas of tidal marshes in the neighbourhood of Freetown, Sierra Leone. Breeding is maximal soon after the onset of the rains, but as these become heavy, the rate declines, to rise again as the rains diminish. Infection has been found in up to 4.7 per cent. The author discusses identification by characters of the adult and of the egg. THOMSON (p 795) gives an account of *A. melas* and *A. gambiae* in West Africa. In transmission the latter is nearly three times as effective as *A. melas* and together, these mosquitoes form a very formidable partnership. *A. melas* breeds in *Avicennia* mangrove near Freetown, but round Lagos and in the Gold Coast it is associated with the great stretches of *Paspalum* grass in the inter-tidal zone. It makes use of fresh water only to a negligible extent, and is therefore confined to the area below high spring-tide mark. THOMSON (p 795) comments on the breeding habits of *A. gambiae* in West Africa, which are not understood. It breeds in streams and in some pools and puddles, but by no means all, and the conditions which render one pool suitable and another not, are not clear. *A. gambiae* remains the most dangerous malaria vector in the world.

JEPSON *et al.* (p 1030) describe the habits of *A. funestus* and *A. gambiae*, the two vectors of malaria in Mauritius, the former is the more important, because it can breed in colder conditions, and throughout the year, whereas *A. gambiae* is restricted to the hot wet season. *A. gambiae* tolerates a high degree of salinity along the coast, but the true *A. melas* has not been found there. *A. funestus* does not tolerate more than a trace of salt. The effect of shade is to reduce breeding of *A. funestus*, but this is probably due to reduction of temperature rather than to the effect of light.

VINCKE (p 163) found a sporozoite index of 7 per cent in *A. duren* caught in the Belgian Congo. This mosquito was not found in houses or stables but formed a high proportion of the anophelines caught in the open.

WOLFS (p 164) describes 9 species of *Anopheles* caught near Coquilhatville, of which *A. moucheti* is probably the most important local vector, endemic malaria is relatively light in this area.

Senior WHITE (p 787) discusses the outside resting places of certain Indian anophelines. It seems that a high proportion are to be found outside at a period of the gonotrophic cycle when it is usually assumed that they are at their feeding sites and therefore susceptible to spray-killing with pyrethrum insecticide. The same author (p 797) sums up the relationship between ricefields and the breeding of *Anopheles* in India. Where *A. annularis* is the vector, all ricefields are dangerous for *A. culicifacies* the danger period is until the plant is 12 inches high, for the *A. fluviatilis* group all non-seepage ricefields are harmless, but seeping ricefields are very dangerous. Fallow fields are also very dangerous in relation to *A. culicifacies* and the *A. fluviatilis* group.

RAJINDAR PAL (p 19) shows that in Delhi the optimum conditions for *A. culicifacies* are temperature of 25°-30°C, and relative humidity from 60 to 80 per cent. This species does not hibernate or aestivate and is not here a habitual feeder on man, it does not usually fly more than half a mile from its

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In a comprehensive report, TREDRE (p 488) describes the breeding habits of *A. melas* in the *Paspalum* grass and *Avicennia* mangrove areas of tidal marshes in the neighbourhood of Freetown, Sierra Leone. Breeding is maximal soon after the onset of the rains, but as these become heavy, the rate declines, to rise again as the rains diminish. Infection has been found in up to 4.7 per cent. The author discusses identification by characters of the adult and of the egg. THOMSON (p 795) gives an account of *A. melas* and *A. gambiae* in West Africa. In transmission the latter is nearly three times as effective as *A. melas*, and together these mosquitoes form a very formidable partnership. *A. melas* breeds in *Avicennia* mangrove near Freetown, but round Lagos and in the Gold Coast it is associated with the great stretches of *Paspalum* grass in the inter-tidal zone. It makes use of fresh water only to a negligible extent, and is therefore confined to the area below high spring-tide mark. THOMSON (p 795) comments on the breeding habits of *A. gambiae* in West Africa, which are not understood. It breeds in streams and in some pools and puddles, but by no means all, and the conditions which render one pool suitable and another not, are not clear. *A. gambiae* remains the most dangerous malaria vector in the world.

JEPSON *et al.* (p 1030) describe the habits of *A. funestus* and *A. gambiae*, the two vectors of malaria in Mauritius. The former is the more important, because it can breed in colder conditions, and throughout the year, whereas *A. gambiae* is restricted to the hot wet season. *A. gambiae* tolerates a high degree of salinity along the coast but the true *A. melas* has not been found there. *A. funestus* does not tolerate more than a trace of salt. The effect of shade is to reduce breeding of *A. funestus*, but this is probably due to reduction of temperature rather than to the effect of light.

VINCKE (p 163) found a sporozoite index of 7 per cent in *A. durem* caught in the Belgian Congo. This mosquito was not found in houses or stables, but formed a high proportion of the anophelines caught in the open.

WOLFS (p 164) describes 9 species of *Anopheles* caught near Coquilhatville, of which *A. moucheti* is probably the most important local vector, endemic malaria is relatively light in this area.

Senior WHITE (p 787) discusses the outside resting places of certain Indian anophelines, it seems that a high proportion are to be found outside at a period of the gonotrophic cycle when it is usually assumed that they are at their feeding sites and therefore susceptible to spray-killing with pyrethrum insecticide. The same author (p 797) sums up the relationship between ricefields and the breeding of *Anopheles* in India. Where *A. annularis* is the vector, all ricefields are dangerous for *A. culicifacies* the danger period is until the plant is 12 inches high for the *A. fluviatilis* group, all non-seepage ricefields are harmless but seeping ricefields are very dangerous. Fallow fields are also very dangerous in relation to *A. culicifacies* and the *A. fluviatilis* group.

RAJINDAR PAL (p 19) shows that in Delhi the optimum conditions for *A. culicifacies* are temperature of 25°-30°C, and relative humidity from 60 to 80 per cent. This species does not hibernate or aestivate and is not here a habitual feeder on man, it does not usually fly more than half a mile from its

breeding place. No morphological differences could be found between specimens caught in areas where *A. culicifacies* is, and those where it is not, a vector.

Senior WHITE and RAO (p. 491) show that *A. annularis* widely spread throughout the East but usually not of much malaria importance is the chief vector in the plains of Orissa, where it finds favourable breeding conditions in village tanks with a heavy growth of aquatic vegetation, and in ricefields during the rains. It can be controlled by attention to the tanks. *A. annularis* breeds in salty waters on the low-lying coast and is a more dangerous vector than *A. annularis*.

VISWAKATHAN (p. 391) describes the relationship between seasonal rainfall, irrigation systems, and the breeding of *A. flavius* in part of Bombay this mosquito is responsible for transmission in the rice and sugar-cane areas. *A. flavius* was the only species found infected in one area of the Southern Central Provinces of India by Senior WHITE (p. 358).

Senior WHITE *et al.* (p. 37) show that *A. flavius*, *A. versus* and *A. minimus* are the chief vectors of malaria in the Jeypore Hills, and have calculated the anthropophilic indices of these and others. They found also that a high proportion of some species survived more than 12 days in the cold weather.

SIMPSON (p. 663) discusses the transmission of malaria by *A. stephensi* in Calcutta, where this species formed 87 per cent. of *Anopheles* caught in houses, and where its total infection rate was 0.85 per cent.

From an analysis of the results of a large trapping experiment in Burma, YORK and FOX (p. 160) conclude that *A. symanskyi* is attracted by man, and hardly at all by animals, whereas *A. ecostus* and *A. philippinensis* are almost entirely animal feeders.

Until recently it had been assumed that the vector of malaria in North Borneo was *A. maculatus* but an investigation made by McARTHUR (p. 788) showed that this assumption could not explain the peculiar distribution of the disease. By careful research, the author was led to suspect *A. leucosphyrus* and this was, in fact, the only anopheline found infected in the area surveyed, although many other species were present. *A. leucosphyrus* breeds in clear seepages under dense jungle shade, and the female visits houses after midnight, and departs after feeding without resting. Control by partial clearing of the jungle, to admit light, gives promise of success.

PERRY (p. 391) reports careful studies of *A. punctulatus farauti*, the chief vector in the New Hebrides and Solomon Islands. It breeds in many kinds of water always open to the sun. Eggs may be laid on mud, and they and the larvae and pupae can withstand partial drying. Details should be sought in the original.

MACKERRAS (p. 642) gives a list of Australasian vectors. The dangerous vectors are *A. punctulatus punctulatus* and *A. p. farauti* [the latter being regarded as a race of *A. punctulatus*]. For the list of potential vectors and those of unknown importance the abstract should be consulted.

YOUNG *et al.* (pp. 275-482) have shown that several North American anophelines including *A. quadrimaculatus* are able to transmit *P. warr* from various other parts of the world. YOUNG and BURGESS (p. 694) have succeeded in transmitting *P. malariae* by *A. maculipennis freeborni*.

A list of anophelines caught during a special survey in Canada is given by TWINN (p. 694). The known vectors, *A. quadrimaculatus* and *A. maculipennis freeborni* were found in various provinces.

ATKIN (p. 693) has given full account of the anopheline fauna of western America, but this cannot be condensed.

PARKHOUSE *et al.* (p. 21) have studied the close relationship between the amount of aquatic or semi-aquatic vegetation and the breeding of *A. quadrimaculatus*. Methods of water management suitable for the control of over 100 plants are

discussed, the most difficult being the alligator weed, which produces a floating mat, and which needs larvicidal oil. The flowering of certain plants gives a readily recognizable indication of the beginning of the anopheline breeding season. GARTRELL and ORGAIN (p 20) note that *A. quadrimaculatus* tended to disperse relatively far from a reservoir on the Tennessee in which it was breeding prolifically. BROOKE and PROSKE (p 22) have prepared a serum by intraperitoneal injection of macerated pupae of *A. quadrimaculatus* into a rabbit. A precipitin test with this serum may be of value in the study of natural enemies of mosquitoes. HUNT and DAVEY (p 694) describe in detail their method of maintaining a colony of *A. quadrimaculatus*. SABROSKY *et al* (p 392) report infection in 3.38 per cent of *A. crucians* in S Carolina, this mosquito is usually considered of relatively slight importance. It feeds actively in November, when *A. quadrimaculatus* is hibernating. FITZGERALD (p 274) reports on malaria in a US naval base in Cuba, where *A. albimanus* is the vector. VARGAS (p 959) reports *A. darlingi* in part of Mexico in which it had not previously been found.

In a study of Brazilian anophelines, DEANE, CAUSEY and DEANE (p 20) have shown that the most efficient indigenous vector is *A. darlingi*, and that *A. aquasalis* becomes important if very numerous. *A. albittarsis* (which may include a number of species) and *A. pessoai* are of secondary importance. Morphological information, and keys, are included in the original papers. PAYNE and SANCHES (p 692) note that *A. darlingi* is the most important vector in the remote areas of Brazil, and FLOCH (p 486) that it is the most important vector in French Guiana, where the maximum incidence occurs in the dry season, and where most of the cases are due to *P. falciparum*. SCHLAVI (p 165) shows that *A. albittarsis domesticus* is the commonest anopheline, and probably the most important vector, at Iguape, on the coast of Brazil, where endemic malaria is severe. CASTILLO (p 276) notes that in Ecuador *A. albimanus*, *A. darlingi* and *A. pseudopunctipennis rivadeneirai* are important vectors. HACKETT (p 276) shows that *A. pseudopunctipennis* which is responsible for much malaria in the Andes, exists up to altitudes of 2,600 metres, he notes that it is probably not a homogeneous species, but consists of several varieties. RACHOU (p 165) reports on the habits of anophelines of the sub-genus *Kerteszia* in part of Brazil, where they show a strong tendency to invade houses. RACHOU and FERREIRA (p 1032) have studied the anophelines (of the sub-genus *Kerteszia*) which breed in bromeliads, in southern Brazil. RACHOU (p 1032) has found infection in *A. cruzi*, *A. bellator* and (probably) *A. homunculus*, of this group.

#### Pathology Clinical Findings

In a comprehensive discussion of the cellular basis for immunity in malaria, TALLAFERRO (p 493) describes the fixed and free macrophages, noting that one effect of acquired immunity is an increased rate of phagocytosis, the local increase in the macrophages is probably a reflection of natural immunity. He discusses the proliferation of various tissues which occurs in malaria. This paper cannot satisfactorily be abstracted. SPITZ (p 1032) describes the post mortem findings in *P. falciparum* malaria. She makes the point that in the brain lesions the vessels are rather distended than obstructed by parasitized erythrocytes though thrombi are occasionally found in vessels associated with haemorrhage. She describes and discusses the findings in the kidneys, but for this the original should be consulted. In discussing the heart lesions observed in fatal *P. falciparum* malaria, MERKEL

(p. 172) comments on the fact that parasitized red cells adhere to capillary walls and that endothelial cells are swollen. The result must be anaemia, and, in fact, the lesions resemble infarcts, for the coronary collateral circulation is poor. Anaemia of the heart may be as important as occlusion of cerebral vessels.

A description of the cytology of bone marrow in malaria is given by LANZA (p. 168). A study of the blood and bone marrow as affected by malaria, is reported by MUKHATCHEVA (p. 494) but details should be sought in the original abstract.

BELTRÁN and DÁVALOS (p. 960) show that examination of fresh blood is efficient for demonstration of malaria parasites as an emergency measure, if staining is impossible.

In discussing splenic indices, GÓMEZ MARCANO (p. 390) makes certain suggestions on matters of detail, which are important. These should be sought in the original abstract.

DELL and KLINEFELTER (p. 171) discuss their radiological studies on spleen size, but their findings should be sought in the original.

TORON (p. 278) and PULLEN (p. 790) report cases of spontaneous rupture of enlarged spleen in malaria.

ZERMATI and VARGUES (p. 869) have found, as others have found, that the complement titre falls during the course of malaria (as in other infections) and rises after cure. In severe cases, persistent absence of complement indicates the probability of a fatal ending—progressive rise in titre preceded cure. This is a non-specific phenomenon, more marked in *P. falciparum* than in *P. vivax* infections.

MAYER and HEIDELBERGER (p. 172) have studied the complement-fixation reaction in malaria, using for the purpose antigens from various plasmodia. For latent malaria the test has only limited value but if syphilis is excluded, a positive reaction is specific for malaria. It seems that the malaria antigens contain a Wassermann antigen which is distinct from them. GORDON *et al.* (p. 173) report that a complement-fixation test with an antigen from *P. gallinaceum* is not of much value in detecting latent malaria.

MELNEY (p. 492) sums up part of the literature dealing with the changes in physiological processes resulting from malaria. He deals, for instance, with blood proteins, blood sugar, blood electrolytes, and anaemia. For details the original should be consulted. GALL and STRICKBERG (p. 878) show that in malaria and in artificial fever there is a fall in serum inorganic phosphorus, and a rise in blood glucose—they discuss the implications of these and related findings.

BIANCO *et al.* (p. 1034) as a result of observations made on 1,300 attacks of malaria in U.S. naval men, make the point that a large proportion of them gave positive reactions with most of the ordinary tests for syphilis, but the tests usually became negative within 4 weeks.

TRIMARCHI (p. 168) reports that Ascoli's adrenalin treatment restores the fixing capacity of the reticulo-endothelial system to normal in malaria, as shown by the results of the Congo red test.

CARLSON *et al.* (p. 174) describe a colorimetric test which may be significant in diagnosis, though it is probably not specific.

MAHARI (p. 279) finds fairly good correlation between the cephalin-cholesterol flocculation test and spleen and liver enlargement in malaria, and that the shorter the infection, the stronger the reaction.

MACHELLA *et al.* (p. 557) report a relationship between retention of injected bromsulphthalein and the intensity of malarial fever.

LIPPINCOTT *et al.* (p. 166) have investigated liver function in patients with induced *P. vivax* malaria, and conclude that although there is some dysfunction

during the attack, this passes off when effective treatment is given. Somewhat similar findings are also reported by GLENN *et al* (p 167). Having performed liver function tests on a series of patients with *P. vivax* malaria, SCHNEIDER and SHALLENBERGER (p 1033) conclude that although there is some evidence of transitory liver damage in a proportion of patients, permanent damage is rare. BUTLER and SAPERO (p 1034) show that American Negroes were as susceptible as white troops to malaria on an island in the South Pacific. LAMBILLON (p 1034) describes patients with lesions resembling erysipelas, apparently resulting from malaria. SPRAGUE (p 25) thinks that the possibility of cardiac damage from recurrent malaria is extremely remote. KARK (p 170) gives reasons for thinking that the risk of activating latent malaria by surgical operations has been somewhat over-emphasized. DI COSTA (p 558) enters the warning that patients with fever of malarial type, who do not respond to anti-malaria treatment, should be examined for tuberculosis.

SIUTE (p 169) defines latent *P. vivax* malaria as an attack in a patient who has been infected several months before the onset of symptoms. The delay may be due to drug suppression, immunity, or infection with two species, or it may be related to the number of sporozoites inoculated, since it occurs only with small numbers. Relapses, on the other hand, are due to activity of the parasites after a resting phase.

From an analysis of the records of malaria in Samarkand, GEVORKOV (p 486) concludes that during the first half of the year 5-12 per cent of the cases are primary infections with long incubation periods.

BELTRAN and SAYDOVUL (p 961) have found that when malaria is induced by injection of infected compatible blood, the incubation period lasts only 1-3 days, but that with incompatible blood it is never less than 5. KAPLAN *et al* (p 281) give advice (which should be sought in the original) as to the best dosage of blood containing *P. vivax* for the induction of therapeutic malaria. KAPLAN *et al* (p 25) have shown that nien infected with *P. vivax* in the Pacific show considerable immunity if re-inoculated with similar strains for the treatment of neurosyphilis, but that with heterologous strains, satisfactory courses of treatment can be given. ENGSTROM *et al* (p 961) report on patients treated in America, for neurosyphilis, by induced malaria with strains from the Pacific and the Mediterranean.

CITTA *et al* (p 561) have hyper-immunized patients submitted to malaria therapy by repeated inoculation of various strains of parasites of the three common species. Tests carried out during 14 years after this procedure indicate that immunity to *P. malariae* lasts longest and may persist after parasites have been eliminated. With *P. vivax* immunity is usually but not always associated with persistence of the parasites. *P. falciparum* gives the least immunity, probably because its antigens act for a short time only, nevertheless a degree of immunity may be detected several years after cessation of activity.

CHRISTIANSON *et al* (p 24) show that in a minority of relapses occurring in the United States of *P. vivax* malaria contracted in the Pacific or the Mediterranean the patient may show parasitaemia without fever for a few days. A few of such patients may have gametocytes in the blood but there is no serious risk of infecting local mosquitoes on a big scale. KITCHEN and PETERMAN (p 23) give detailed observations on the character of the parasites of mosquito induced malaria with the McCoy strain of *P. vivax*. These cannot satisfactorily be abstracted further.

In discussing the characteristics of *P. vivax* malaria in children in the Panama Canal Zone, FISHBEIN (p 695) remarks that cerebral and algid forms

(p. 172) comments on the fact that paratized red cells adhere to capillary walls, and that endothelial cells are swollen. The result must be anaemia, and, in fact, the lesions resemble infarcts, for the coronary collateral circulation is poor. Anaemia of the heart may be as important as occlusion of cerebral vessels.

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CANAPERIA, G A *Malaria in Italy during the War and Post-War Period.*  
*Bull Office Internat d'Hyg Publique* 1946, Oct-Nov-Dec, v 38,  
 Nos 10-11-12 1070-76 [French version 1062-9]

As a result of antimalaria measures, the progressive reduction of malaria morbidity and mortality in Italy culminated in 1940 when the figures were the lowest ever recorded 55,453 cases and 488 deaths as compared with 249,529 cases and 11,477 deaths in 1918. The recent war had a disastrous effect on the malaria situation. The destruction of bridges preventing the free flow of water and resulting in marsh formation, the destruction of dykes and drainage works producing vast inundations, increasing difficulty in maintaining antilarval work, the dispersal of trained staff engaged on antimalaria work, the progressive scarcity of antimalaria drugs, overpopulation of endemic areas in which living conditions were precarious, the presence of non-immune troops in endemic areas who became infected, and the systematic removal of cattle by the enemy, were all factors responsible for greatly increased malaria incidence. This increase occurred wherever the two chief vectors of Italian malaria were present—*A. maculipennis labranchiae* in central and southern Italy, Sicily and Sardinia, and *A. sacharovi* along the coast-line of Venetia and Emilia. In areas where the much less important vectors *A. maculipennis* and *A. m. atroparvus* or *A. m. messeae* predominated there was no marked exacerbation of the disease. In 1942 the registered number of cases and deaths had risen to 164,082 and 1,075, in 1944 to 373,941 and 422 and in 1945 to 411,602 and 386.

Since the cessation of hostilities energetic antimalaria measures have been restarted with the cooperation of UNRRA and the Rockefeller Foundation. Conditions have improved. In certain areas DDT has been used with great success. A vast plan of control with DDT in all endemic areas was decided upon, in collaboration with UNRRA. The Rockefeller Foundation is directing a scheme for the eradication of anophelines from Sardinia by the use of DDT.

Norman White  
 [Change-  
*Riv di Malariaologia*  
 1947, Apr, v 27, No 2, 74-9 [12 refs] English summary (7 lines)]

FERRARO, F *Variazioni anofeliche nel bacino del Basso Volturno* [War destruction in the Volturno Delta undid the work of years of effort. Bridges, roads and canals were wrecked with the result that the country reverted to conditions that characterized it before bonification. The author reports on the results of an anopheline survey and on the saline content of water in breeding places. *A. maculipennis labranchiae* remains the most prevalent and important vector in the district, but *A. sacharovi* has appeared in places in which it had not previously been reported.]

BULL INST HYG MAROC 1945, v 5, 85-95 1 chart *Rapport annuel du Service Antipaludique en 1945* [Annual Report of Antimalaria Service, Morocco, in 1945]

Norman White

Morocco suffered less than usual from malaria in 1945. During the summer months malaria was less in evidence than were relapsing fever and numerous intestinal infections aggravated by scarcity. In the few localities however where conditions favoured anopheline propagation severe outbreaks of malaria were made more deadly by destitution. The year was abnormally dry after January. The annual number of cases of malaria treated by dispensaries etc from 1940 to 1943 approximated 300,000. In 1945 it was 160,000. This figure is an overstatement, because at the

and that children respond well to treatment with mepecrine. ENKOWSK and TOMLINSON (p. 363) show that in children admitted to hospital in the Panama Canal Zone for malaria, more than half had *P. falciparum* infections—most of the cases were from rural or semi-rural areas.

PERVIZ (p. 277) has found that congenital *P. falciparum* infections are by no means rare in the French Cameroons, yet clinical manifestations are not observed in infants up to the age of 2 months. Malaria is responsible for much of the high infant mortality.

KRAM and TAYLOR (p. 166) report cases of the algal form of *P. falciparum* malaria, in which the signs of shock (with haemo-concentration) responded to fluid replacement therapy with plasma, blood or intravenous fluids.

HILLS (p. 169) reports 24 cases of malarial jaundice, in 5 of which the infection was with *P. vivax* and in 19 with *P. falciparum*. This appears to be haemolytic jaundice and rapid haemolysis may cause haemoglobin to appear in the urine. BIRNBAUM *et al.* (p. 22) show that red cells from patients with malaria are laked in bile solution more easily than normal cells, and that although quinine, atabrin and plasmoquine all accelerate this haemolysis, quinine administered *per os* to normal subjects does not do so.

BROCK *et al.* (p. 230) state that as American Negroes are often refractory to *P. vivax* *P. malariae* should be used for therapeutic purposes. A daily parasite count is desirable in therapeutic malaria—they note that with *P. falciparum* counts of 100 000 to 200 000 per cmm. are on the danger line. This last infection was rarely used.

FISCHER and YORK (p. 25) report transfusion malaria from blood donors who gave histories of quartan malaria 36–42 years before. Charles W. Weeks

[To be continued]

## MALARIA

- J. NATIONAL MALARIA SOC. 1947 Sept. v 6, No. 3 203-16. [19 refs.]  
 Medical Research in Malarology in the First Postwar Year 1945-46.  
 Report of the Committee on Medical Research [HAAS V. H. Chairman]

More than 100 institutions or individuals in the United States and abroad were asked for information regarding medical research in malarology that was being actively prosecuted in 1945-46. The information received is summarized in this report. Thirty-one laboratories in the United States reported on their investigations—these cover all aspects of the subject. The development and testing of new anti-malarial drugs is receiving most attention. Avian strains of malaria are very widely employed. In the United States, 15 laboratories were using avian parasites, 8 were using human and 7 simian parasites. *Plasmodium gallinaceum* was most frequently used. About half the laboratories in the United States were maintaining mosquitoes.

The response to requests for information lead the Committee on Medical Research to conclude that exchange of information regarding programmes and progress of research would be welcomed by all malarologists.

No significant diminution of the intensified medical research in malarology that characterized the war years had become apparent. It is pointed out, however, that the great majority of U.S. laboratories engaged in this work are dependent to a considerable extent on Federal government financial support.

Vernon White

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Norman White

FERRARO, F *Variazioni anofeliche nel bacino del Basso Volturno* [Chang-  
 ing Anopheline Prevalence in the Volturno Delta] *Riv di Malarologia*  
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War destruction in the Volturno Delta undid the work of years of effort. Bridges roads and canals were wrecked with the result that the country reverted to conditions that characterized it before bonification. The author reports on the results of an anopheline survey, and on the saline content of water in breeding places. *A maculipennis labranchiae* remains the most prevalent and important vector in the district but *A sacharovi* has appeared in places in which it had not previously been reported.

Norman White

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beginning of the outbreak of relapsing fever many cases of that disease were labelled malaria.

Routine antilarval activity was maintained. In 1,004 positive slides examined in the central laboratory there were *P. falciparum* 321 *P. malariae* 319 *P. vivax* 164

Norman White

SCHWITZ, J. with the collaboration of H. RAUMANN Mme. BRUMER & M. FORT  
Recherches sur le paludisme dans la bordure orientale du Congo Belge.  
[Investigation of Malaria along the Eastern Frontier of the Belgian Congo.]  
Institut Royal Colonial Belge. Section des Sciences Naturelles et Médicales.  
Mémoires. (Collection in-8°) 1944 v 14 No. 3 216 pp. 9 maps (1  
folding) & 42 figs. on 8 pls. [18 refs.]

This volume sets out in much detail the results of a tour of investigation into malaria conditions along the eastern frontier of the Belgian Congo, undertaken on behalf of the Belgian Royal Colonial Institute. The tour embraced the shores of Lake Kivu and the high plateaux surrounding the lake Rutshuru and its neighbourhood, between Lake Kivu and Lake Edward, the Semliki Valley between Lake Edward and Lake Albert and the high plateaux overlooking it from the west Kasenyi and neighbourhood, on the south-eastern shore of Lake Albert, Irumu and the gold mines at Kilo. The main objects of the tour were the verification of the belief that the high plateaux are free from endemic malaria, the determination of the altitude at which such freedom becomes operative, and the study of malaria in mines and plantations among labourers who had been recruited from high altitudes. Recent reports had ascribed outbreaks of sickness, with considerable mortality to malaria, on grounds which the author considered to be altogether insufficient.

In nearly all the numerous localities visited, a study was made of anophelines, adults and larvae. Blood preparations, both thick drop and smear were made from 6,841 individuals. The formidable task of examining these films was carried out in Brussels after the return of the mission.

No evidence of indigenous endemic malaria was found in Rugari (1 700 metres above sea level) Butembo (1 750) Kadifedje (2,150) Kabare (1,950) Numbi (2,200) and Ngweshu (1 700). Endemic malaria was, however found in Nyangesi (1,650 metres) which is very close to Ngweshu south-east of Lake Kivu. The line of demarcation is between 1 700 and 1,800 metres above this, there is no endemic malaria. At the higher altitudes such redoubtable African malaria vectors as *A. gambiae*, *A. fuscipes* and *A. marshalli* were never found, though other anophelines, notably *A. christyi* and very occasionally *A. knygi* and *A. transvaalensis* were sometimes plentiful. *A. christyi* is evidently of no importance as a malaria vector.

Special attention was given to two mining areas, Kaduba-Mufwa and Monghwatu and an agricultural district Rutshuru, where severe outbreaks of malaria had been reported. In none of these areas was there evidence of acute malaria, other than a few mild cases, but in one camp Bwat Moko, blood examinations revealed a state of subacute malaria. There were no febrile reactions but there was a very heavy infection of adults with *P. malariae* and a notable proportion of *P. vivax*, parasites which in Africans, in endemic areas, are restricted to the early years of life, before the acquisition of premonition. Such findings indicate malaria of recent origin.

The author briefly indicates some of the many unsolved problems of malaria in Africa that await elucidation, and recalls the recommendation made by him in 1936 to the Malaria Commission of the League of Nations for a coordinated programme of research to be carried out in the different African colonial territories. [See also this Bulletin, 1947 v 44 783.]

Norman White

SCHWETZ, J, BAUMANN, H & FORT, M Nouvelles recherches sur les anophèles et le paludisme endémique dans l'agglomération de Coquilhatville (Congo belge) [New Investigation of Anopheles and Malaria in Coquilhatville, Belgian Congo] *Ann Soc Belge de Méd Trop* 1947, Mar 31, v 27, No 1, 139-59, 1 map

The unusually low endemicity of malaria in the neighbourhood of Coquilhatville, where *A. gambiae* was not found and where *A. marshalli* var *moucheti* was the most common anopheline, has previously been described by the authors [this *Bulletin*, 1939, v 36, 777, 1943 v 40, 103]. They now present the results of another brief survey carried out in November, 1945.

*A. gambiae* was still absent from Coquilhatville though it appeared, in small numbers, in neighbouring villages, *A. marshalli* var *moucheti* was still the predominant anopheline. The authors subscribe to the opinions expressed by WOLFS that the stratum of limonite (bog-ore) that lies on or near the surface acts as a deterrent to the breeding of *A. gambiae* [this *Bulletin* 1947, v 44, 164]. Blood examinations once more showed a very low prevalence of malaria parasites were very few in positive smears. *P. vivax* was not found and *P. malariae* was rare. Gametocyte carriers were very infrequent. *A. marshalli* var *moucheti* is evidently a much less effective vector of malaria than *A. gambiae*.  
Norman White

REBELO, A O sezonismo em Quelimane [Malaria in Kilimane] *An Inst Med Trop* Lisbon 1946, Dec, v 3, 143-58, 1 fig English summary

Kilimane is a small town in Portuguese East Africa, in the coastal plain that lies to the north of the mouth of the Zambezi River. Next to scabies and yaws, malaria is the most prevalent disease. Among a population of 2 077, the annual number of malaria cases registered, between 1941 and 1944, varied from 881 to 2,129. The spleen rates of children in different parts of the town ranged between 58 and 77 per cent, and the parasite rates between 47 and 66 per cent. The percentages of plasmodia found in films were *P. falciparum* 97.9, *P. malariae* 2.7 and *P. vivax* 2.2. Of 573 anophelines captured in dwellings, *A. funestus* formed 71 per cent, the remainder were *A. gambiae*. The sporozoite rates were *A. funestus* 3.1 (157 dissections) *A. gambiae* 5 per cent (60 dissections).  
Norman White

FAUST E C, SCOTT, J A & McDANIEL, G E Malaria Mortality and Morbidity in the United States for the Year 1945 *J National Malaria Soc* 1947 Sept, v 6, No 3, 184-91, 2 figs

Previous reports in this series showed the considerable increase in malaria mortality in the United States that synchronized with the economic depression of the mid-1930's and the subsequent substantial yearly decrease in mortality in practically every malarious State. During the recent war years, conditions were complicated by the establishment of large military centres in highly malarious areas and the return of innumerable military personnel and prisoners of war from hyperendemic malarious areas overseas. In spite of these conditions the 1945 civilian malaria mortality figures are highly satisfactory. The total civilian deaths for 1945 numbered only 399, as compared with 584 in 1944 and 622 in 1943. In 1935, there were 4,268 certified deaths from malaria, meanwhile the population has increased perhaps 10 per cent. There are still hyperendemic malaria areas in the south-eastern States, in the Mississippi valley, in eastern Oklahoma and Texas and in the lower Rio Grande. Case-reporting of malaria is insufficient to provide accurate information of

the distribution and intensity of the disease, except in the States of South Carolina, Mississippi and Texas.

As in previous years, the basic data were obtained from the bureaux of vital statistics of each of the States.

Norman White

PIREÑO GARCÍA, P. P. Endemiografía del paludismo en la provincia de Santa Fe. [Distribution of Malaria in the Province of Santa Fe.] *Kuba*. Habana. 1947 Apr., v 3 No. 4, 95-8.

This paper contains a general description of the distribution of malaria in Argentina and a more detailed description of the topography and malaria incidence in the Province of Santa Fe. This province occupies the territory between the Paraná River and the eastern frontier of Argentina. It contains 19 departments grouped into northern central and southern zones. During nine years 2,497 cases were registered in the Province, 2,002 of these being in the northern zone. One of the northern departments, General Obligado was alone responsible for 1 622 cases, 916 of them in a single year 1941. *P. vivax* is the prevailing type of infection. It is probable that most if not all of the cases reported from the central and southern zones were relapses of infections acquired in the northern zone or elsewhere.

Norman White

DRANE, L. M. Observações sobre a malária na Amazônia brasileira. [Observations on Malaria in the Amazon Region, Brazil.] *Rev. Serviço Especial de Saúde Pública*. Rio de Janeiro. 1947 v 1 No. 1 3-60 3 maps & 3 graphs. [30 refs.] English summary

This report gives a summary of observations made by the Special Public Health Service between July 1942 and June 1946 on the distribution and transmission of malaria in the Amazon Region of Brazil. This huge territory of some 3 600,000 square kilometres comprises 41.5 per cent. of the total area of Brazil but has an estimated population of only one and a half million. The observations included the examination of 185,214 blood films and 43 496 spleens in 76 localities the results of which are tabulated. The over-all parasite rate was 3.1 per cent. the spleen rate 12.8 per cent. There were striking differences in the degree of malaria endemicity in different parts of the territory. The incidence of species of *Plasmodium* in the positive blood slides was *P. vivax* 83.2 *P. falciparum* 36.6 and *P. malariae* 0.2 per cent.

The examination of 562,054 adult anophelines and 1,300 734 larvae from 115 localities revealed the presence of 30 species and varieties, which are listed. The only important vectors of malaria are believed to be *A. darlingi* and *A. aquasalis*. The former was found throughout the region. *A. aquasalis* was confined to coastal districts. *A. albopictus* var. *domesticus* was very abundant in some areas but did not appear to be as important a vector in the Amazon as it is reputed to be in other parts of Brazil.

House-spraying with DDT-kerosene solution promises to be a valuable control measure for *A. darlingi*. [See also this Bulletin 1948 v 43 287.]

Norman White

PIREOTTI, M. A malária no Brasil. [Malaria in Brazil.] *Folha Med.* 1947 June 25 & July 5 v 28 Nos. 12 & 13 156 pp. 13 figs. & 2 maps.

A description is given of the constitution, organization and functions of the National Malaria Service of the National Health Department of the Ministry of Education and Health of Brazil, which was inaugurated in 1941. It consists of an Epidemiological Section, a Section of Organization and Control, a

Section of minor hydraulic engineering work, an Administration Section, and an Institute of Malariology

A list is given of all localities in all the *municípios* of Brazil from which endemic malaria has been reported, this list occupies 132 pages. Fifty-four species of anophelines have been identified in Brazil. The distribution of these according to States is presented in graphic tabular form. Apart from *A. gambiae* which, imported from West Africa, played an important localized rôle in the transmission of malaria until it was eliminated, eight species have been found naturally infected with malaria, *A. darlingi*, *A. albistarsis*, *A. tarsimaculatus*, *A. strodei*, *A. noroestensis*, *A. (Kerteszia) cruzi*, *A. (K.) bellator* and *A. (K.) homunculus* (?). This also applies to *A. noroestensis*. The three importance as a vector. Though widely distributed, is probably of little or no practical species of *Kerteszia* are limited to the States of São Paulo, Paraná, Santa Catarina and Rio Grande do Sul, where bromeliads provide facilities for their breeding. *A. darlingi* is the most redoubtable vector of all. The report gives some illustrations of excellent drainage work of several species of bromeliads and of the work being done to control *Kerteszia*.

WHITE, R. Senior, RAMAKRISHNA, V. & RAO, V. V. *Malaria on the North Madras Coast*. Indian J. Malariology 1947, Mar., v 1, No 1, 81-109, 1 graph [11 refs] Norman White

The area dealt with in this report is a narrow coastal plain between the Eastern Ghats and the Bay of Bengal, from the Rushikuliya River southward to the Vamsadakra River. It is mostly not more than ten miles in width. Only two rivers traverse the plain both rise from the eastern face of the Ghats and are seasonal in their flow. Until ten years ago, this area of India was reputed to be completely free from malaria. In 1938 *A. sundaus* was discovered in the coastal village of Naupada, associated with malaria prevalence. Each year thereafter until 1945, extensions and tabulated reports. These findings are summarized and tabulated. In some places in the area, *A. stephensi* is the malaria vector, in others both *A. stephensi* and *A. sundaus* are responsible. Reports on the salinity of *A. sundaus* breeding places are summarized. It would seem that salinity as low as 100 parts per 100,000 is the optimum for oviposition, but no less than 50 per cent of the total larval production occurs in waters with a salinity between 700 and 1,000 parts per 100,000. These findings suggest the existence of two races of *A. sundaus*. The freshwater race is possibly a more efficient vector than the other. Further evidence is adduced favouring the hypothesis that two races exist. Norman White

RAO T. R. *Visual Responses of Mosquitoes artificially rendered Flightless*. J. Exper. Biol. 1947, Sept., v 24 Nos 1/2, 64-78, 6 figs

Normal mosquitoes are known to avoid the light in the daytime but most of them tend to fly out of their dark shelters at dusk. This paper describes experiments with mosquitoes (*Culex molestus* and *Anopheles maculipennis atroparvus*) prevented from flying by amputation of the wings or by fixing the wings together. It was thought that this method would allow more accurate measurement of their responses. It was found that the mosquitoes, placed in a small arena illuminated from below, would always walk towards a dark section of the wall. This

occurred wherever the black band was placed in their field of vision, provided that it was sufficiently wide to subtend an angle of 8° on the mosquito's eye.

Contrary to expectations, there was no change in the insect's avoidance of light at dusk. About 10 per cent. of the mosquitoes were slightly abnormal in their directional response towards the black band but only one out of all the specimens investigated actually moved towards the light.

J R BURRIS

VOGT G B Salinity Tolerance of *Anopheles quadrimaculatus* and Habitat Preference of *A. crucians bradleyi* J Econom. Entom. 1947 June, v 40 No 3 320-25.

The purpose of this paper is to establish for one locality a carefully defined example of appreciable salinity tolerance of *Anopheles quadrimaculatus* which is generally regarded as a distinctly freshwater anopheline. Notes on *A. crucians bradleyi* and *Culex salinarius* are also included.

The investigation was made in the vicinity of Scotland, St. Mary's County Maryland, U.S.A. Sampling stations in Deep Creek were selected because they gave a range of salinities from minimum to maximum values. The sampling methods and characteristics of the creek are described.

Larvae were found in the north arm of the creek where salinity ranged from 1,400 to 2,800 ppm. soluble chlorides but they did not occur in the south arm where the salinity was from 4,400 to 8,300 ppm. although the pH and the plant coverage were similar in both places. On one occasion in the south arm, larvae were found after an original salinity of 2,900 ppm. soluble chlorides had increased to 5,200 ppm. but these were survivors whose development had begun at the lower salinities. From the results of the observations which are summarized in four tables, it is concluded that the salinity tolerance of *A. quadrimaculatus* may be as high as 2,900 ppm. soluble chlorides.

The only other mosquitoes associated with *A. quadrimaculatus* were *A. crucians bradleyi* and *Culex salinarius*. The distribution of the larvae of these two species seemed to be unrelated to salinity. They were found in the marshy ground between the two arms of the creek only in the spring and autumn were they collected from the exposed water surface associated with the Sago pond-weed.

H S LECHE

RACHOU R G & FERREIRA, M O As *Aedes* como os grandes responsáveis pela malária no litoral do Estado de Santa Catarina. [The *Aedes* Mosquitoes as Prominent Vectors of Malaria in Littoral of the State of Santa Catarina, Brazil.] *Folia Med.* 1947 Jan. 5 v 28, No. 1, 8 pp.

MACGRAITH, B., ANDREWS W H H & GALL, D A Hepatic Syndrome of Wide Distribution Illustrated by Lesions in Malaria and Blackwater Fever *Lancet.* 1947 Nov 29 781-4 [73 refs.]

In fatal cases of malaria, necrosis of the liver cells occurs in the inner two-thirds of the lobule, being most prominent in the cells surrounding the central veins and sinusoids, which may be deeply congested. This hepatic lesion resembles that resulting from right-sided heart failure associated with tissue anoxia arising from interference with escape of venous blood from the liver. As right-sided heart failure is not a feature of malaria, some other factor must be involved in the obstruction to the outflow from the liver of venous blood. Histological evidence gives no support to obstruction by agglutination of red



cells, thrombosis or degenerated Kupffer and littoral cells. The authors suggest that in malaria, blackwater fever and various other conditions in which the same lesions arise from stagnant anoxia, the obstruction to the venous flow from the liver is brought about by reflex constriction of some part of the hepatic venous tree. It is difficult to understand why the anoxia should affect the cells at the centre of the lobule only, but it is supposed that some process exists which permits the peripheral cells to remove the oxygen from the blood. The constriction is brought about by nervous reflexes which may have their origin within or outside the liver. If arising outside the liver, they probably account for the relationship between hepatic and renal disturbances.

C M Wenyon

DUBOIS, A. Observations sur la pathologie paludéenne chez les indigènes de Pawa (Nepoko) [Observations on the Pathology of Malaria among the Natives of Pawa (Nepoko)] *Ann Soc Belge de Méd Trop* 1947, Mar 31, v 27, No 1, 17-24

The author has noted a much higher incidence of splenomegaly among adult females than among adult males in Pawa, Belgian Congo. There is no other evidence that females suffer more from malaria than males. The phenomenon appears to be due to the greater relaxation of visceral ligaments and of the abdominal wall that characterizes the female. In routine examinations the spleen is palpated with the patient standing. The splenic index may thus be misleading unless it be confined to children. The curve of age incidence of malaria in Pawa differs somewhat from that found in most other parts of the Belgian Congo at similar altitudes. Pawa is 800 metres above sea-level. Maximum spleen and parasite rates are attained at slightly older ages, this is attributed to the relatively low anopheline density in Pawa.

Norman White

WHORTON, C M, PULLMAN, T N, KIRSCHBAUM, W R, JONES, R Jr, ALVING, A S, CRAIGE, B, Jr, EICHELBERGER, Lillian & COULSTON, F. The Chesson Strain of *Plasmodium vivax* Malaria IV Immunity *J Infect Dis* 1947, July-Aug, v 81, No 1, 1-6, 2 figs [25 refs]

In previous communications, the authors have described certain characteristics of induced malaria with the Chesson strain of *P. vivax*, of New Guinea origin [this *Bulletin*, 1948, v 45, 139-40]. In this paper, immunity acquired from such infection is described. In 135 primary attacks of sporozoite-induced infections, the onset of fever occurred when the average parasite count was 10 parasites per cmm. With the first and second relapses, there was a progressive increase in the parasite density at the onset of fever, but with the third relapse the pyrogenic threshold did not differ significantly from that of the second. Similarly, in trophozoite-induced infections the threshold at the onset of clinical reactivation was higher than at the onset of the first period of clinical activity. In trophozoite-induced infections, peak parasitaemia was noted on the 12th day on the average with a range of 5 to 46 days. Parasite densities were higher than those reported with indigenous strains, the mean maxima in 95 patients being 33,000 parasites per cmm of blood (2,600 to 90,000). Negroes were refractory to infection with trophozoites. In white subjects, acquired immunity, to both homologous and heterologous strains, was demonstrated.

Norman White

The first patient was happily married, free from worries, and from any history of mental disorder. She received a total of 1.8 gm. of mepacrine over four days for the treatment of a proved *P. falciparum* infection and responded so rapidly that she felt well on the fourth day. She retired to bed at 9.30 and chatted, apparently cheerfully and normally with her husband the next morning, the husband awoke to find that his wife had disappeared. Her body was found soon after in the river and death was shown to be due to drowning, without evidence of other abnormalities.

The second patient had suffered from claustrophobia after shell-shock during the 1914-18 war but had recovered by 1924. He had also suffered recently from subtertian malaria and had 1.0 gm. of mepacrine in 5 days, followed by 10 grains of quinine bishydrochloride t.d.s. from the sixth to the tenth day. On the sixth evening the patient felt sick after taking quinine, and on the seventh, without medical advice, he reverted to mepacrine (0.1 gm. t.d.s.). On the evening of the ninth day (after he had taken a total of 2.4 gm. of mepacrine) the patient went to his bath at 8 p.m. where he felt feeling of unreality coming over him. He then found himself sitting, naked and wet, in his dining-room and this amnesia lasted for about half an hour. Immediate stoppage of mepacrine resulted in no further ill-effects [see also FINDLAY this Bulletin, 1947 v 44 763].

H. J. O'D. Burke-Gaffney

HOOKER, S. W. Psychotic Reactions to the Ingestion of Large Doses of Quinacrine in Normal Subjects. *Amer J Trop Med.* 1947 July v 27 No. 4 477-81

Thirty-one medical, dental and medical administrative corps officers volunteered to take quinacrine (mepacrine) at first in suppressive and then in therapeutic dosage. None had ever had malaria, nor were they in an endemic area. The dosage was 0.1 gm. daily for 12 weeks. 0.1 gm. twice daily for one week and finally 0.4 gm. three times one day 0.3 gm. three times the next day and 0.1 gm. three times daily for the next four days. Twenty-four of these officers developed toxic central nervous system symptoms varying from mild insomnia and depression to severe psychotic reactions in three cases. The symptoms subsided promptly on discontinuing the drug. The most toxic reactions occurred in two persons with a previous history of depression episodes. The worst and most prolonged effect occurred in the case of an officer who exceeded the above dosage. He took 0.5 gm. instead of 0.3 gm. on the third (? second day) of intensive dosage. The earliest manifestations of cerebral toxicity are insomnia, restlessness, increased dreaming, and mild depression or elation. [See above]

[This work may be compared with the extensive observations made on volunteers by the British Army Malaria Research Unit see MARGRAITH & HAYARD this Bulletin, 1945 v 42, 863.]

Norman White

See also p. 288 WILLIAMS, The Tropical Lisbon Plague Syndrome.

CLAVERO G. ROMEO VIANCONTE, J. M. & LOZANO A. Tratamiento del paludismo con paludrina. (Primeros ensayos en España.) [Treatment of Malaria with Paludrine: First Trials in Spain.] *Rev. Habana.* 1947 Aug v 3 No. 8 183-5

Twelve cases of acute malaria, ten *P. vivax* and two *P. falciparum* infections, were treated with paludrine. The dose given to adults was 0.10 gm. thrice daily for five or six days. The symptoms were relieved and asexual parasites disappeared from the peripheral blood in less than 60 hours in all cases.

Norman White

AFRIDI, M K, RAMAKRISHNAN, S P, GOSWAMI, A & MENON, M K An  
*Enquiry on certain Aspects of Paludrine* Indian J Malariology 1947,  
 Mar, v 1, No 1, 221-9

This describes an inquiry to determine the optimum single dose of paludrine for the control of the clinical symptoms of malaria. For this purpose two villages, Kechi Beg and Ahmad Kanzai, four and six miles south of Quetta, Baluchistan, were selected. Here malaria is highly endemic, but the transmission season is of only about 12 weeks' duration. The spleen rates in these villages were 23.6 (June) and 69.6 (September), and the parasite rates 1.97 and 4.3 per cent respectively. The inquiry lasted from July 6 to October 2. Villages were preferred to a hospital, for this inquiry, because the follow-up of patients presented fewer difficulties. A single-room hut in the centre of each village served as a dispensary, patients were received daily six days a week. Patients suffering from fever, with malaria parasites in their blood, were treated with either (1) One tablet of paludrine, 100 mgm, (2) a single dose of 3 tablets, 300 mgm, (3) two tablets of paludrine twice a day as long as the patient attended (up to 3 days), or (4) three tablets of mepacrine a day in two doses as long as the patient attended (up to 3 days).

Altogether, 563 patients were treated, records regarding the day of disappearance of fever and parasites are available for 241 cases. The single dose treatments with either 100 or 300 mgm paludrine caused abatement of fever and disappearance of parasites within 3 days, in a high proportion of cases. Multiple doses in treatment (3) gave no significantly better results than treatment (2). Mepacrine gave no better results than treatments (2) and (3) although a slightly smaller proportion of patients treated with mepacrine returned with second attacks. The conclusion was that the optimum single dose of paludrine to obtain a clinical cure of a malarial attack was 300 mgm.

Norman White

SS INSTITUTE OF TROPICAL HYGIENE (INDIA BRANCH) Report to the Committee of Control of the Ross Institute (India Branch) on the Control of Malaria in Industrial Labour Forces in India [MACDONALD G, M D, D P H, D T M, Director of the Ross Institute of Tropical Hygiene, Keppel Street, Gower Street, London, W C 1] pp iii+72, 8 figs 1947

One of the objects of an extensive tour made by the author in the north-east and south of India was to enquire and report on the extent to which recent developments in malaria control can be economically adapted to the needs of industry in India. It was clear that recent developments could not be considered without regard to existing practices with which they must be integrated. The result is this very useful pamphlet which deals with the whole subject of malaria control in this part of the world, with special reference to new weapons which wartime research has made available, new antimalarial drugs, DDT, Gammaxane, etc. The pamphlet is not intended for the expert malariologist. It is concise and clear and should be of great value to medical officer and layman alike who are concerned with these problems and who have an elementary knowledge of malaria.

In the parts of India with which the author is concerned, the most important malaria vectors are *A. minimus*, *A. philippinensis*, *A. culicifacies* and *A. fluviatilis*, but many of the author's recommendations are of general application, whatever the vector may be.

It appears that DDT in India has been discredited, chiefly on account of the grossly inadequate quantities that had been applied. This arose from the

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H J O'D Burke-Gaffney

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Norman White

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Norman White

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*Norman White*

ROSS INSTITUTE OF TROPICAL HYGIENE (INDIA BRANCH) **Report to the Committee of Control of the Ross Institute (India Branch) on the Control of Malaria in Industrial Labour Forces in India** [MACDONALD, G, M D, DPH, DTM, Director of the Ross Institute of Tropical Hygiene, Keppel Street, Gower Street, London, W C 1] pp iii+72, 8 figs 1947

One of the objects of an extensive tour made by the author in the north-east and south of India was to enquire and report on the extent to which recent developments in malaria control can be economically adapted to the needs of industry in India. It was clear that recent developments could not be considered without regard to existing practices, with which they must be integrated. The result is this very useful pamphlet which deals with the whole subject of malaria control in this part of the world, with special reference to new weapons which wartime research has made available, new antimalarial drugs, DDT, Gammexane, etc. The pamphlet is not intended for the expert malariologist. It is concise and clear and should be of great value to medical officer and layman alike, who are concerned with these problems and who have an elementary knowledge of malaria.

In the parts of India with which the author is concerned, the most important malaria vectors are *A. annulus*, *A. philippinensis*, *A. culicifacies* and *A. fluviatilis*, but many of the author's recommendations are of general application, whatever the vector may be.

It appears that DDT in India has been discredited, chiefly on account of the grossly inadequate quantities that had been applied. This arose from the

fact that preparations containing DDT and not DDT itself had been purchased and then diluted excessively. The warning is timely.

Jaswant Singh's modification of Field's quick staining method, for thick and thin blood films, is described and strongly recommended. The preparation of the stain is clearly described.

Norman White

WOODRUFF A. W. The Suppressive and Schizonticidal Value of Paludrine (100 mg.) in Vivax Malaria. *Trans Roy Soc. Trop Med. & Hyg* 1947 Oct. v 41 No. 2, 263-7 1 chart.

Twenty patients suffering from *P. vivax* malaria were treated with paludrine. Most of the patients were ex-prisoners of war from the Far East. All had had previous attacks of malaria, varying in number from one to twenty; most had had relapses since repatriation. Each patient admitted to hospital for a malaria attack was treated with a single tablet of 100 mgm. of paludrine only. On discharge from hospital, each patient was given 25 of these tablets with instruction to take one each week. A year after admission to hospital, that is, six months after the completion of the paludrine course, a questionnaire was sent to each patient asking for information about long-term and short-term relapses.

During the acute attack, the response to a single dose of paludrine was slow but the attack was controlled in all cases. The temperature fell to normal in 12 hours in only 7 of 15 cases. In 3 cases the febrile period lasted more than 48 hours after the administration of the drug. The dose of 100 mgm. is probably sub-optimal and should be increased.

During the period of 6 months in which the patients were receiving 100 mgm. paludrine weekly, one relapse was seen and three other possible clinical attacks were reported.

During the 6 months immediately after the 6 months of suppressive paludrine, there was one long-term relapse and one other possible clinical relapse.

No toxic manifestations were seen at any time.

Norman White

KENNEY M. & BRACKETT S. The Effectiveness of Metachloridine in suppressing Natural Infections with *Plasmodium malariae* and *P. falciparum* in British Guiana. *Amer J Trop Med.* 1947 July v 27 No. 4 493-501 [11 refs.]

Metachloridine (2-metanilamido-5-chloropyrimidine) was tried as a suppressive of malaria in British Guiana. For this purpose four schools in the neighbourhood of New Amsterdam were selected. The children in these schools are children of labourers on sugar estates. Negroes and East Indians are about equally represented. The schools are in a flat coastal area where suitable breeding places for *A. darlingi*, the chief vector, abound.

The treated group and the control group each consisted of 250 children. Treatment lasted from February 4 to April 17 and from May 6 to July 28, 1948; the interval was the Easter holiday. Up to May 30 each treated child received the appropriate proportion of the adult dose, one gramme per week, divided into 2, 3 or 5 parts; the weight of the child determined the dose. On May 30 the dosage was doubled. Blood smears were examined just before treatment was started, immediately after the Easter holiday, 50 days after the termination of treatment and at intervals of 3 weeks during treatment.

Before treatment, 9 of the control group and 8 of the treated group harboured *P. malariae*. During treatment, there were 58 positive *P. malariae* slides (35 children) in the control group; none in the treated group. Metachloridine is a highly effective suppressant of *P. malariae*.

During treatment, there were 93 positive *P. falciparum* slides (60 children) in the control group, 37 (24 children) in the treated group. The reduction in *P. falciparum* parasitaemia as compared with the control group was 40 per cent during the period of one gramine dosage, and 72 per cent with two grammes. No symptom of toxicity was ever seen.

There were 11 positive *P. vivax* slides in the control group, only one in the treated group, possibly owing to failure to take the drug. *Norman White*

FRANIS, B. V. Relative Effectiveness of various Repellents against *Anopheles farauti* Laveran. *J. National Malaria Soc.* 1947, Sept., v. 6, No. 3, 180-83.

Tests were done at Guadalcanal with a small cage, and at Efate with a large insectary. Volunteers exposed their treated and untreated limbs simultaneously to this mosquito, and noted the times for the first bite on the treated areas.

An earlier paper (Franis *et al.*, *J. Econom. Entom.*, 1946, v. 39, 627) showed that while one compound was the most effective repellent for a certain biting insect, another might be better against a different insect. The present paper provides more data to support this conception because the standard repellents dimethyl phthalate and Indalone were found to be of only moderate value against *A. farauti*. The compound R 612 (2 ethyl-1,3-hexanediol) and certain other substances (such as undecylenic acid) were much better.

It was concluded that a mixture of repellents was more satisfactory than any single one. The 6:2:2 mixture (dimethyl phthalate R 612 and Indalone) was fairly satisfactory against *A. farauti*. *J. R. Busvine*

TONKING, H. D., LAVOIEFERRE, R. & COURTOIS, C. M. A Small Scale Experiment in the Use of DDT in Mauritius. 5 pp. 1946. Port Louis. J. H. Bowkett, Govt. Printer. (10 cents.)

In a small scale experiment during the period December, 1945 to March, 1946 the authors demonstrated to their own satisfaction that DDT applied as a residual insecticide (5 per cent DDT in kerosene) to the type of labourer's dwelling found in Mauritius resulted in a pronounced reduction in the numbers of *A. farauti* and *A. gambiae* caught by hand in those dwellings. The procedure was welcomed by the populace concerned and it was decided to experiment further on a larger scale to determine the effect of this residual insecticide on the incidence of malaria. [See below.] *R. Ferd. Fréde*

TONKING, H. D. & GIBERT, S. The Use of DDT Residual Sprays in the Control of Malaria over an Area of 16 Square Miles in Mauritius. *Medical and Health Department Mauritius Central Laboratory, Publication No. 10*

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cycle It is known that *G pallidipes* feed less freely than *G swynnertoni* under most conditions, but more frequently in the dry season

[The plural of proboscis is repeatedly given as "proboscidae" Surely an editor should be prepared to adjust an error of this nature] P A Buxton

NASH, T A M A Record of *Syntomosphyrum glossinae* from Nigeria *Bull Entom Res* 1947, Dec, v 38, Pt 3, 525

Some 23 years ago LLOYD *et al* [this *Bulletin*, 1927, v 24, 891] attempted unsuccessfully to introduce the Chalcidid pupal parasite *Syntomosphyrum glossinae* into a part of Northern Nigeria as a measure of control of tsetse flies [A similar experiment had been tried with little success by LAMBORN in Nyasaland (*ibid*, 1925, v 22, 291)] It is suggested that the seasonal high temperature and low humidity were responsible for the failure of the experiment

The present author now records that in April 1947, the laboratory stock of *Glossina palpalis* puparia from the Kaduna area (which is 210 miles south-west of Sherifuri, where LLOYD *et al* had experimented, in breeding sites of *G morsitans* and *G tachnoides*), suddenly became heavily infested with *S glossinae* It is presumed that an infected pupa had been brought in from the bush and had initiated the mass infestation of the offspring

The author concludes that *S glossinae* is indigenous in Nigeria and that its presence cannot be attributed to the abortive efforts of LLOYD *et al* twenty-three years ago

[The reference to LLOYD and JOHNSON given by the author appears to be incorrectly quoted it presumably refers to LLOYD, JOHNSON and RAWSON (*Bull Entom Res*, 1927, v 17, 423, referred to above) and not to "Lloyd and Johnson (*Bull Entom Res* 27, p 449, 1927)" as stated by the author]

H J O'D Burke-Gaffney

GLASGOW, J P & DUFFY, B J The Extermination of *Glossina palpalis fuscipes*, Newstead, by Hand Catching *Bull Entom Res* 1947, Dec, v 38, Pt 3, 465-77, 2 maps & 5 figs on 1 pl

The paper describes a successful eradication of *G palpalis* from a narrow water-side fly belt, by catching with nets

The authors worked on the river Sari in South Kavirondo, Kenya. About sixteen miles of river was infested with *G palpalis* They isolated two stretches of river-side vegetation by removing light bush, and used them for experiment and control The two stretches were thus isolated by clearings of 5 000 yards or over In one area of infested bush (3,800 yards long, about fifteen yards wide on each bank), fly-rounds were carried out for three months, and showed about sixty "total flies per 10,000 yards" Then ten teams of fly boys (three in each team, with a hessian screen) were brought in to catch flies this is equivalent to two teams per 1,000 yards of stream In the first six months they caught 282, 84 and 33, 2, 4 and 1 Meanwhile the standardized fly-round figure fell from about sixty to six or lower from the first month of catching Further study, including intensive attempts to catch flies, repeatedly showed no evidence of reinfestation up to seventeen months

Meanwhile in the other isolated stretch of fly-bush, where catching had not been undertaken, *G palpalis* continued to be common

Investigations were also carried out in the area in which SYMES and VANE [see this *Bulletin*, 1937, v 34, 542] carried out the first "catching out" experiment which had appeared successful and seemed to have controlled human trypanosomiasis. These areas had only been isolated by riverside clearings of about 1,000 yards Reinfestation had occurred, though the density of the flies was very low [which seems to suggest a recent reinvansion]

blood-induced infections. Sulphachiarine only was used in prophylactic experiments administration spread over four days was again more effective than a more intense medication, as judged by the number of parasitized red cells present on the fifth day. It was doubtful whether sterilisation occurred with this drug its action on blood forms and pre-erythrocytic forms appeared to be about the same. The four-day treatment as generally employed appears, on the whole, to have distinct advantages. J D Fallon

RIMINGTON C. & FULTON J D with the assistance of H. SHEINMAN. The Pigment of the Malarial Parasites *Plasmodium knowlesi* and *Plasmodium gallinaceum*. *Biochem. J.* 1947 v 41 No. 4 619-22, 5 figs. on 1 pl. [16 refs.]

1 The pigment of malarial parasites (*P. knowlesi* and *P. gallinaceum*) has been extracted by a technique which avoids the use of alkali at all stages.

"2. From this material, crystalline haem and pyridine haemochromogen have been prepared.

3 A comparison of the spectral absorption of malarial pigment and of haemin in different solvents and of the visible bands and Soret bands of haemoglobin derivatives made by combining these pigments with renatured or globin confirms the identity of both malarial pigments with haematin (ferriprotoporphyrin)."

### TRYPANOSOMIASIS

HEGH, E. Lee tá-tá. Description-biologie-moyens de destruction.

This book is reviewed on p. 275

VANDERPLANK, F L. Some Observations on the Hunger-Cycle of the Tsetse-Flies *Glossina swynnertonii* and *G. pallidipes* (Diptera) in the Field. *Bull. Entom. Res.* 1947 Dec. v 38, Pt. 3 431-8, 1 fig.

The author wishes to know whether the interval between a tsetse's successive meals is longer at one season than another.

The method used is to estimate the hunger stage of the live fly. Those males which are captured in stage 1 (replete, recently fed) or stage 4 (very hungry) are marked with distinctive spots of paint the tip of the proboscis is snipped off to prevent further feeding and the insect is released. On subsequent days a considerable proportion of marked flies are recaptured and the hunger stage which they have reached is recorded.

The type of result obtained may be illustrated by the results with *G. swynnertonii* for December. Of flies released in stage 4 (very hungry) fifteen were recovered in the two subsequent days and none later. Flies released in stage 1 (replete) had reached stage 4 when recaptured between the 4th and 11th day (mean 7.35 days 23 individuals). From data of this type the author concludes that at that season, flies released when very hungry and unable to feed, carry reserves of food and water sufficient for two days or less. Those which were replete did not require to search for food for a number of days, and were therefore recaptured after about a week.

The paper contains similar data for *G. swynnertonii* for eight successive months, with monthly data on wind velocity saturation deficiency and evaporation also for *G. pallidipes* on a less extensive scale. It is conclusively shown that the mean hunger cycle of both species varies with season, is significantly correlated with measurements of humidity and is shorter when humidity is low or evaporation high. Under the conditions which prevailed, seasonal differences in temperatures were slight and without appreciable effect on hunger

was used and the injection was made up to 15 to 20 ml by the addition of normal saline, this was given very slowly. Most patients had paroxysms of coughing, leading to vomiting in a few instances, and one patient developed toxic jaundice two days after the injections. One developed pneumonia as a complication.

Three patients were Indian seamen and three were Englishmen who had served in India during the War. The three Indians responded well to treatment and were apparently cured but were not followed up. Of the three Englishmen, one was cured with a single course; he was known to be well five months later, one responded well to the treatment, but within three months the symptoms recurred and he still had leishmania in his sternal puncture material, he was apparently cured by a second course. The third was quite unaffected by the treatment; he was subsequently successfully treated with pentamidine.

The authors conclude that, although the treatment does not compare with that by neostibosan, urea stibamine, or the diamidines, where a rapid course is required and cost is an important consideration, this treatment might be recommended, since this course occupies two days only against 8, 30, and 12 days, respectively, and the cost is less than that of any of them. *L E Napier*

**NAPIER, L E** Intensive Treatment of Kala-Azar with Sodium Antimonyl Tartrate [Correspondence] *Lancet* 1947, Dec 20, 928

In a letter to the *Lancet*, referring to a paper by ADAMS and SEATON see above, the reviewer pointed out that he had used sodium antimonyl tartrate in the treatment of leishmaniasis since 1917, until 1923 almost exclusively, since there was no better drug available. For the relatively high mortality, which was the rule among patients under treatment for kala azar in those years, sodium antimony tartrate could not be exonerated from responsibility. If therefore experiments were to be made in concentrating the course of treatment he thought that one of the benign pentavalent compounds should be chosen rather than this relatively toxic trivalent salt. The only justification for the choice of sodium antimony tartrate was its extremely low cost. *L E Napier*

**HABIBI** Quelques formes cliniques du bouton d'Orient observées en Iran [Some Clinical Forms of Oriental Sore in Iran] *Cahier Méd Union Française* Algiers 1947, Oct, v 2, No 13 607-9 12 figs

A note with photographs of 12 cases

**GOLDMAN, L** Types of American Cutaneous Leishmaniasis—Dermatological Aspects. A Review *Amer J Trop Med* 1947, Sept, v 27, No 5, 561-84, 12 figs [33 refs]

Cutaneous leishmaniasis is a disease of some importance to North American dermatologists on account of the frequency with which isolated cases appear at dermatological centres, and also because it exhibits certain features of special interest to those studying the immuno-biology of the skin.

The development of cutaneous leishmaniasis can be expressed as follows —

Inoculation  $\longrightarrow$  papule  $\longleftrightarrow$  ulcer  $\longrightarrow$  scar

A simple general classification for primary American cutaneous leishmaniasis is —

I Cutaneous II Mucosal, (a) primary, (b) metastatic III Mixed

The author, however, prefers Rabello's classification —

I Cutaneous

A Ulcerative (i) impetiginoid, (ii) ecthymatoid, (iii) true ulcer

B Non-ulcerative (i) nodular dermal, (ii) vegetant, (a) framboesoid or (b) verrucose

In conclusion, the authors emphasize that hand-catching speedily reduces *G. palpalis* to a low figure, and would therefore be expected to check an epidemic. They state that it is much cheaper than clearing [It is essential to give cost in money and man days, in describing work of this type, and to state what items are included or excluded from the figures. The authors refer several times to cheapness in a purely qualitative way] P. A. Buxton

### LEISHMANIASIS

HEILIG R. & SACHDEV R. N. Kala-Azar in Jalpur *Indian Med Gaz.* 1947 June 82, No. 6 336-9

It is generally agreed that the incidence of kala azar which is high in Eastern India, declines rapidly as one traces its extension westwards, but authors show differences of opinion on its westerly limit. Jalpur is in any case outside the recognized endemic area.

The authors report nine cases and claim that their report "confirms the experience that wherever one looks for kala-azar one shall find some. The cases were selected on account of positive aldehyde tests and enlarged spleens.

In two cases, leishmaniae were found by sternal puncture. In a third the sternal-puncture findings were doubtful and in three others negative. In the doubtful case and in two of the three negative cases, there was strong clinical evidence, including response to antimony to support the diagnosis of kala azar. However each of these five patients, in whom there was unequivocal or strong evidence of kala azar had lived at some time in a recognized endemic area three within a year of one eighteen months before and one seven years before coming under observation. The last two were the patients in whom leishmania were found. Of the other four patients, in whom the evidence was limited to a large spleen and liver and a ++ aldehyde reaction, three had never left Jalpur and one was a nomad.

The authors conclude: We are unable therefore, to make a definite statement whether kala azar of undoubted Jalpur origin exists, being not sure whether a fully positive aldehyde test, not corroborated by the presence of Leishman-Donovan bodies in sternal smears, is sufficient for establishing this diagnosis.

[The aldehyde test is of great value in a highly endemic area, especially for out-patient use when large numbers of patients are involved, and in these circumstances a definite positive reaction is sufficiently strong evidence for treatment to be undertaken. It is, however a non-specific test and the diagnosis should always be confirmed by the demonstration of leishmania if data are to be used for scientific purposes, e.g. appraising the value of a specific drug or upsetting preconceived ideas regarding the geographical distribution of the disease.] L. E. Napier

ADAMS, A. R. D. & SEATON D. R. Intensive Treatment of Kala-Azar with Sodium Antimonyl Tartrate. *Lancet.* 1947 Oct. 18, 575-8.

Encouraged by the success of ALVES and BLAIR [this *Bulletin* 1946, v. 43 344] with intensive administration of sodium antimonyl tartrate in the treatment of schistosomiasis, the authors decided to try this treatment in six cases of kala azar.

Sodium antimonyl tartrate was given intravenously. The total dosage was about 1 grain per 12 lb. of body weight, divided into six doses given over a period of two days usually at 9 a.m. noon and 3 p.m. A 2 per cent. solution

CHEVE, J, COURDURIER, J & SAISSAC, R Typhus de laboratoire Intérêt des épreuves de contrôle pour le diagnostic des maladies inapparentes [Laboratory Typhus The Use of Control Tests for the Diagnosis of Inapparent Attacks] *Bull Soc Path Exot* 1947, v 40, Nos 9/10, 315-16.

Among 60 laboratory workers exposed every day to risk of infection, 12 suffered from recognizable attacks which were confirmed by Giroud's intradermal reaction and by rickettsia-agglutination tests Four inapparent attacks were detected by the same means

All the workers had been protected by the Durand-Giroud vaccine Rickettsiae could not be recovered from any of the patients *John W D Megaw*

FERRO-LUZZI, G & FERRO-LUZZI, S Therapeutic Study on Louse Borne Typhus *Boll Soc Ital di Med e Igiene Trop* (Sez Eritrea) 1947, v 7, Nos 1/2, 5-23, 2 figs [25 refs]

The authors have carried out tests of 17 special methods of treatment of typhus fever, of which they have observed 2,480 cases in a hospital in Eritrea during a period of about eight years commencing in February, 1939, half of the patients were employed as controls

The treatments tested included most of those for which claims of efficacy have been made, but they did not include *para*-aminobenzoic acid, which was not available

No significant benefit was observed except in the case of aspirin which was given in divided doses amounting to 4.0 to 8.0 gm daily

Among 95 patients treated with the drug only two died, and one of these was moribund on admission The fatality rate among the controls was 14.8 per cent The average duration of the fever among the treated was 11.1 days; among the controls it was 14.8 days Complications and untoward effects among the treated were 23.8 per cent, and 20.2 per cent among the controls A striking improvement is said to have occurred in nearly all the treated patients soon after the commencement of the treatment

[In view of many disappointments in the past, it is necessary to subject the methods of control to a close scrutiny, on this point the evidence supplied in the paper is incomplete and conflicting]

It is stated that "As far as possible the treatments were tried in alternate cases", but a little later the authors mention that selection of cases for treatment was governed "by the two following criteria, early stage of illness and high degree of severity" It also appears that the same group of patients formed the controls for tests of aspirin and three other drugs Detailed information is given of only two groups of patients, those receiving 4.0 gm aspirin daily, and those receiving 8.0 gm daily, from this it appears that in the former group, consisting of 40 patients, only one was over 30 years old and in the latter, consisting of 55 patients, no less than 20 were over 30

In view of the above evidence, the method of control cannot be regarded as satisfactory, and as aspirin was the last method tested it seems possible that the drug was tried towards the end of the epidemic season, though the authors state that the average severity of the attacks was much the same in the first as in the second half of the epidemic period during which aspirin was tested]

*John W D Megaw*

- II Subcutaneous ("pro parte")
  - A. Non-ulcerative
  - B. Secondary ulcerative
- III Mucosal
  - A. Vegetant—non-ulcerative
  - B. Vegetative—ulcerative
- IV Mixed various combinations of above.

The special character of American cutaneous leishmaniasis is mucosal involvement. This is of two types, primary or by direct extension from a cutaneous lesion and metastatic. The mucosal lesion does not occur in Mexico, it is uncommon in Costa Rica, but common in Peru. Extensive lesions resulting from neglect of early metastatic mucosal infections are common in adults, in contrast to the cutaneous lesions which are commoner in children over the age of six months. Weiss gives the frequency of mucosal involvement in Peru as from 20 to 80 per cent. according to the region. Mucosal lesions are usually in the respiratory tract especially the nasal septum.

Clinical diagnosis is always difficult. The location of the lesion on an exposed part of the body the chronicity and the response to antimony treatment help clinical diagnosis. In differential diagnosis gummata, chronic pyodermitis of the tropical ulcer type cutaneous diphtheria, artefactual lesions, and the infectious granulomata have to be taken into consideration. The last-named includes sporotrichosis, blastomycosis, chromoblastomycosis, paracoccidioidomycosis, yaws, syphilis granuloma inguinale (granuloma venereum) rhinoscleroma lupus vulgaris leprosy and stasis syndrome.

Parasitological diagnosis is also difficult. Smears are best obtained by pipette aspiration at the periphery of the lesion. Culture on N.N.N medium can also be obtained by this procedure. Casual scraping of the lesion is useless. Histological study of biopsy material is of little value non-specific inflammatory and tuberculous reactions are observed, and only rarely are intracellular parasites identified by this means.

The author discusses the inter-relationship between Old World and New World cutaneous leishmaniasis or visceral leishmaniasis and the factors which bring about the variations in the clinical types of American leishmaniasis. These include virulence of the organism, vector relationships, tropism secondary infections and natural and acquired constitutional factors. He considers that there are great opportunities for investigation in this direction.

Treatment is reviewed, but no special recommendations are made and there is a paragraph on prevention.

It is a stimulating article, if somewhat untidy and quite inconclusive. It should be read in the original by those especially interested in this disease.

There are a large number of excellent photographs illustrating the types of cutaneous leishmaniasis and the conditions from which it must be distinguished.

L. E. N. per

## FEVERS OF THE TYPHUS GROUP

HOITLIK, G. A. & SHEPARD, C. C. Effect of Egg Yolk on Release of Antigen from Rickettsiae. *Proc. Soc. Exper Biol. & Med.* 1947 Oct. v 68 No. 1 146-8. [12 refs.]

"The addition of as little as 2.5 per cent egg yolk to suspensions of yolk sacs infected with the rickettsiae of epidemic and endemic typhus fever Rocky Mountain spotted fever and rickettsialpox (*R. prowazeki*, *R. mooseri*, *R. rickettsii* and *R. akari*) prior to treatment with ether has resulted in antigens with enhanced titers as measured by the complement fixation test.

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Among 95 patients treated with the drug only two died, and one of these was moribund on admission The fatality rate among the controls was 14.8 per cent The average duration of the fever among the treated was 11.1 days, among the controls it was 14.8 days Complications and untoward effects among the treated were 23.8 per cent, and 20.2 per cent among the controls A striking improvement is said to have occurred in nearly all the treated patients soon after the commencement of the treatment

[In view of many disappointments in the past, it is necessary to subject the methods of control to a close scrutiny, on this point the evidence supplied in the paper is incomplete and conflicting

It is stated that "As far as possible the treatments were tried in alternate cases", but a little later the authors mention that selection of cases for treatment was governed "by the two following criteria, early stage of illness and high degree of severity" It also appears that the same group of patients formed the controls for tests of aspirin and three other drugs Detailed information is given of only two groups of patients, those receiving 4.0 gm aspirin daily, and those receiving 8.0 gm daily, from this it appears that in the former group, consisting of 40 patients, only one was over 30 years old and in the latter, consisting of 55 patients, no less than 20 were over 30

In view of the above evidence, the method of control cannot be regarded as satisfactory, and as aspirin was the last method tested it seems possible that the drug was tried towards the end of the epidemic season, though the authors state that the average severity of the attacks was much the same in the first as in the second half of the epidemic period during which aspirin was tested]

*John W D Megaw*

NELIS, P. La prophylaxie du typhus exanthématique en Belgique de 1940 à 1946. [The Prophylaxis of Exanthematic Typhus in Belgium from 1940 to 1946.] *Arch. Belges Méd. Sociale Hyg. Méd. du Travail et Méd. Légale*. 1946 Aug. 4 No. 6 298-315.

The interest of this article is chiefly historical. The systematic application of effective methods of control was remarkably successful in preventing any serious outbreaks of typhus fever in Belgium in spite of the repatriation of 284,000 Belgians from Germany and the passage through the country of a large number of persons of other nationalities who also came from Germany.

The total number of cases in 1944 was 10 of which 7 occurred in one infected focus. In 1945 there were 140 cases, but no less than 133 of the patients arrived in Belgium within the incubation period of the disease.

The author claims that the chief lesson to be learned from the success of the preventive measures adopted is the supreme importance of an organization based on a fully staffed and well-equipped laboratory. *John W. D. Megeer*

FLOCH H. & CAMAIN R. Sur les fièvres typhoexanthématiques en Guyane Française. [Typhus Fevers in French Guiana.] *Institut Pasteur de la Guyane et du Territoire de l'Inana. Publication No. 136* 1947 July 4 pp.

In reporting a case of fever of the typhus group in 1941 (Publication No. 10 March 1941) the authors, working in the Pasteur Institute of French Guiana, concluded that these fevers did not constitute a simple problem in Guiana. They have therefore carried out systematic Weil-Felix tests from 1940 to the early part of 1943 on 3,732 sera submitted to the Pasteur Institute monthly for sero-diagnosis for syphilis and on 609 sera sent for Widal reactions.

The suspensions tested were *Proteus* OX19 Metz and Syria and Kingsbury H. and O. The first 2,438 of the 3,732 sera tested at a dilution of 1/50 gave 99 (4 per cent.) positive results the remaining 1,294 at 1/100 gave 29 (2 per cent.) there were thus 128 (3 per cent.) positives by these criteria.

High titres were rare and the positive results fell into two groups, namely those in which agglutination occurred with *Proteus* Metz and Syria only and those in which agglutination with the Kingsbury variants also occurred. The first group constituted 57 per cent. and the second 43 per cent. of all positive findings.

Among the 609 sera sent for Widal reactions, in febrile patients, 25 (4 per cent.) agglutinated the various *Proteus* suspensions at a titre of 1/100 this is about twice the percentage which was found in the case of sera of non-febrile patients.

The authors then describe a case of fever in a European aged 30 which clinically resembled one of the typhus group. All the agglutination tests were negative, except that against the Syrian strain of *Proteus* OX19 which was positive 1/300. The authors therefore examined the patient's serum further by the rickettsia agglutination technique of Giroud, with formalinized suspensions of murine and epidemic strains. This test was positive 1/5,000 with the murine and 1/2,000 with the epidemic strain a later specimen examined by Dr Giroud gave titres of 1/2,560 (and 1/5 120±) for the murine and 1/300 (and 1/340±) for the epidemic strain.

Many rats were found in broad daylight in the patient's house especially in the kitchen. The authors therefore confirm that murine typhus exists in French Guiana, especially in Cayenne, and that another fever of the typhus group, possibly tick borne is also present. *H. J. O'D. Burke-Gaffney*



- VARELA, G & MAZZOTTI, L Dos mamíferos *Dasyprocta novemcinctus* y *Neotoma fuscipes canescens* susceptibles al tifo murino [Infection of *Dasyprocta novemcinctus* and *Neotoma fuscipes canescens* with Murine Typhus] *Rev Inst Salubridad y Enfermedades Trop Mexico* 1947, June, v 8, No 2, 125-7

By means of guinea-pig experiments the authors, working in Mexico, were able to produce experimental infection with murine typhus of the armadillo, *Dasyprocta novemcinctus* and the field rat *Neotoma fuscipes canescens*

H J O'D Burke-Gaffney

- RAYNAL, J H Le chat dans l'épidémiologie du typhus exanthématique murin [The Cat in the Epidemiology of Murine Typhus Fever] *Bull Soc Path Exot* 1947, v 40, Nos 9/10, 367-75 [13 refs]

Murine typhus infection was detected in three out of 25 cats examined in Shanghai during 1942, which was a year of exceptional prevalence of typhus fever among the human and rat population

The author suspects that human beings who come into close association with cats may occasionally become infected through contact with dried faeces of infected fleas harboured by the cats. He thinks, however, that in ordinary conditions cats help to control infection by keeping down the rat population

John W D Megaw

- SOUTHCOTT, R V Observations on the Epidemiology of Tsutsugamushi Disease in North Queensland *Med J Australia* 1947, Oct 11, v 11, No 15, 441-50, 5 figs [15 refs]

Early in this paper, the author states that it is generally accepted that a diagnosis of tsutsugamushi disease should be based on the agglutination of *Proteus OXK* at a titre of 1-160 or, if this level should not be reached, on a rising-titre agglutination [but see the next abstract]

An opportunity occurred of investigating the incubation period of the disease in the Atherton Tableland and the adjoining coastal area of North Queensland. In 34 cases, the date of infection was ascertained, in 26 of these the incubation period was 11-13 days, in the remaining 8 cases it was 14-18 days. The author concludes that in Australia the period is of the order of  $13 \pm 2$  days.

The effectiveness of dibutyl phthalate as a preventive was strongly suggested by the distribution of the eschars, nearly all of which were on parts of the body not adequately protected by the treated clothing. One of the three cases of typhus seen in the coastal area north of Cairns was diagnosed as North Queensland Tick Typhus.

Evidence was found supporting the view that birds are important in spreading larval mites, and that lizards, in the Cairns region, are a major factor in maintaining the population of the vector mites.

John W D Megaw

- HEASLIP, W G Observations on the Epidemiology of Tsutsugamushi Disease in North Queensland [Correspondence] *Med J Australia* 1947, Nov 1, v 2, No 18, 558

In a letter, HEASLIP challenges the diagnostic criteria referred to in the preceding paper, he states that in his own experience mouse inoculations have established the diagnosis of rickettsial infection in several cases in which the *Proteus OXK* reaction remained negative, in one such case, the serum was tested at intervals over a period of 28 days.

John W D Megaw

KHAN N. Early Diagnosis of Tsutsugamushi. *Indian Med. Gaz.* 1947 July v 82, No 7 381-3.

The difficulties in the early diagnosis of scrub typhus are emphasized but certain signs and symptoms, viz., headache, lethargy and apathy vacant expression stare of the eyes deafness of the nerve type hypoplasia fundal changes and blood picture and early morning remissions are helpful."

SNYDER, F. M. & MORTON, F. A. Benzyl Benzoate-Dibutyl Phthalate Mixture for Impregnation of Clothing. *J. Econom. Entom.* 1947 Aug., v 40 No. 4 586-7

Experiments previously reported [this *Bulletin*, 1946, v 43, 1196] indicated that benzyl benzoate and dibutyl phthalate are both good repellents for use against the mite *Entomobrya* and related genera. The former compound appeared to be slightly more effective than the latter but in view of supply difficulties, tests were done with a 50:50 mixture of the two in order to see if this would be adequate.

Experiments showed that the 50:50 mixture was nearly as good as the pure benzyl benzoate in "mite stopping time" and in practical repellence trials, and somewhat more persistent in an ageing test.

J. R. BURRIS

BUSTAMANTE, M. E. & VARELA, G. IV. Estudios de fiebre manchada en Mexico. Papel del *Rhipicephalus sanguineus* en la transmisión de la fiebre manchada en la República Mexicana. [Studies of Rocky Mountain Spotted Fever in Mexico.] *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1947 June, 8, No. 2 136-41 1 map. English summary (3 lines)

The authors were able to produce typical and specific experimental infections of Rocky Mountain spotted fever in guinea pigs inoculated with material from injected *Rhipicephalus sanguineus* collected from different parts of Mexico. They conclude that this tick plays an important rôle as a vector of *R. rickettsii* in that country.

H. J. O'D. BURKE-GAFFNEY

TENDEIRO, J. Ixodídeos da Guiné Portuguesa. Subfamília Amblyomminae. Novo-Lisboa 1938. [The Ticks of Portuguese Guinea: Sub-family Amblyomminae.] Reprinted from *Boi. Cultural da Guiné Portuguesa*. 1947 July No. 7 617-709 31 figs. [22 refs.]

This paper is largely of interest other than medical, but there is a full description of *Haemaphysalis leachi* which is considered by THEILER to be a vector of Tick-bite fever.

H. J. O'D. BURKE-GAFFNEY

## YELLOW FEVER

STEFANOPOULO, M. G. J. & DUVOLON, S. Mlle. Sur l'utilisation du cobaye dans l'étude expérimentale du virus de la fièvre jaune et en particulier du virus atténué de culture (souches 17 D). [Use of the Guinea pig in the study of Yellow Fever Virus, especially Attenuated Strains.] *Bull. Soc. Path. Exot.* 1947 v 40 Nos. 7/8, 285-94 7 text figs. & 4 figs. on 2 pls. [15 refs.]

During the recent war the authors undertook this study of the effect of various strains of yellow fever virus in the guinea pig because of the scarcity of monkeys which are commonly used in testing the neurotropic properties of batches of yellow fever vaccine.

It was found that the attenuated 17D virus (used for vaccine) killed about 40 per cent of guineapigs when inoculated intracerebrally, animals weighing less than 350 gm were more susceptible than heavier ones. Ten passages of the vaccine virus through mouse brain, followed by 7 to 16 passages in chick embryos, failed to increase the virulence of the virus. In addition to those animals which died, some developed paralysis and recovered and others had an inapparent infection which was detected either by reinoculation with virulent virus or by testing for neutralizing antibodies in the blood.

The histological lesions resembled those found after inoculation with the neurotropic strain of yellow fever, but the latter virus produced a more rapidly progressive illness with a mortality of nearly 100 per cent. Thus, the guineapig may be used to detect potential neurotropism of the attenuated 17D vaccine virus. However, the rhesus monkey remains the most suitable animal for this purpose, for it is also capable of detecting return of the attenuated virus to full viscerotropism.

F O MacCallum

HERRERA, G & PARDO, V. A New Method for Biopsy of the Liver. *Arch Pathology* 1947, Oct, v 44, No 4, 393-5, 1 fig.

"A method of obtaining liver for biopsy is described which makes it possible to obtain a cylinder of tissue as long as the distance covered by the trocar in the liver and of the same thickness as the diameter of the trocar. A wire loop at the end of the trocar is an essential feature of the instrument.

"The trauma is minimal, abundant tissue is obtained in every case.

"We have obtained biopsy specimens from 72 patients without a single hemorrhage or other complication."

DE CAIRES, P F. DDT and *Aedes aegypti* Control in British Guiana. *Puerto Rico J Pub Health & Trop Med* 1947, June, v 22, No 4, 405-15, 5 figs [Spanish version 416-24].

British Guiana is the last place of call of northbound air and sea traffic from South America. The control of *Aedes aegypti* in the thickly populated coastal zone, as a yellow fever preventive measure, is rendered very difficult by the complex system of rainwater storage for drinking purposes. A controlled experiment on familiar lines was carried out to determine the efficacy of DDT applied as a residual insecticide. That the very domestic *Aedes aegypti* is most susceptible to 5 per cent DDT in kerosene is clearly demonstrated in that eradication of the species was attained 13 weeks after the single spraying, and maintained for 10 months. A 2½ per cent solution was less effective. It is believed that this method applied on a large scale will be more economical than routine anti-*aedes* measures of control. [See also this *Bulletin*, 1946, v 43 1136, 1947, v 44, 658, 994.]

R Ford Tredre

## DENGUE AND ALLIED FEVERS

LE GAC, P. La ponction lombaire thérapeutique de blocage de la dengue [Lumbar Puncture as a "Block" Treatment of Dengue]. *Bull Soc Path Exot* 1947, v 40, Nos 9/10, 336-9, 5 charts.

The author and SERVANT [this *Bulletin*, 1940, v 37, 273] have already reported that lumbar puncture at any stage of an attack of dengue was found to cause the immediate and complete disappearance of the signs and symptoms of the disease.

KHAN N. Early Diagnosis of Tsutsugamushi. *Indian Med. Gaz.* 1947 July v 82, No 7 381-3.

The difficulties in the early diagnosis of scrub typhus are emphasized but certain signs and symptoms, viz. headache, lethargy and apathy, vacant expression, stare of the eyes, deafness of the nerve type, hypopnea, fundal changes and blood picture and early morning remissions are helpful.

SNYDER, F. M. & MORTON, F. A. Benzyl Benzoate-Dibutyl Phthalate Mixture for Impregnation of Clothing. *J. Econom. Entom.* 1947 Aug., v 40 No. 4 596-7

Experiments previously reported [*this Bulletin* 1946 v 43 1186] indicated that benzyl benzoate and dibutyl phthalate are both good repellents for use against the mite *Eutrombicula* and related genera. The former compound appeared to be slightly more effective than the latter but in view of supply difficulties, tests were done with a 50:50 mixture of the two in order to see if this would be adequate.

Experiments showed that the 50:50 mixture was nearly as good as the pure benzyl benzoate in mite stopping time and in practical repellence trials, and somewhat more persistent in an ageing test.

J. R. BURRIS

BUSTAMANTE, M. E. & VARELA, G. IV. Estudio de fiebre manchada en Mexico. Papel del *Rhipicephalus sanguineus* en la transmisión de la fiebre manchada en la República Mexicana. [Studies of Rocky Mountain Spotted Fever in Mexico.] *Rev. Inst. Salubridad y Enfermedades Trop. Mexico*, 1947 June, v 8 No. 2, 139-41 1 map. English summary (3 lines).

The authors were able to produce typical and specific experimental infections of Rocky Mountain spotted fever in guinea-pigs inoculated with material from infected *Rhipicephalus sanguineus* collected from different parts of Mexico. They conclude that this tick plays an important rôle as a vector of *R. rickettsii* in that country.

H. J. O'D. BURKE-GAFFNEY

TENDEIRO, J. Insetídeos da Guiné Portuguesa. Subfamília *Amblyomminae* Neveu-Lemaire 1938. [The Ticks of Portuguese Guinea: Sub-family *Amblyomminae*.] Reprinted from *Bol. Cultural da Guiné Portuguesa*, 1947 July N. 7 617-709 31 figs. [23 refs.]

This paper is largely of interest other than medical, but there is a full description of *Haemaphysalis leachi* which is considered by THAILER to be a vector of Tick-bite fever.

H. J. O'D. BURKE-GAFFNEY

## YELLOW FEVER

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## Plague

Vol 45, No 3]

species in terms of infection potential, vector potential and transmission potential. According to Burroughs, the vector efficiency thus obtained represents only an approximation to natural efficiency and he points out that this is inevitable because ignorance of ecology precludes the duplication of natural conditions. He uses the well-known statistical formula  $\bar{X} \pm K\alpha \sqrt{\frac{S^2}{N}}$  in order to

find the range within which the true value probably lies, "to estimate the expected number of mice killed (total number of daily transmissions) per flea where  $\bar{X}$  is the average number of transmissions per flea for the entire number of fleas studied,  $N$  the total number of fleas used in the studies," and  $\alpha$  "the probability that the estimating interval covers the true value." In this way, it was found that the true vector efficiency, with a confidence of 90 per cent, of important fleas could be given as —*Xenopsylla cheopis*  $0.660 \pm 0.234$ , *Nosopsyllus fasciatus*  $0.213 \pm 0.157$ , *Orchopeas sexdentatus*  $0.170 \pm 0.138$ , *Diamanus montanus*  $0.02 \pm 0.02$ . The low value and inefficiency given to this last flea, which is grouped with *Opisodasys nesiotis*, *Megabothris abantis* and *Malariaeus telchinum*, is not supported by the work of WHEELER and DOUGLAS [loc cit] who regard it as an exceptionally good vector ( $0.840 \pm 0.232$ ) and more efficient than *X. cheopis*. This, it is suggested by Burroughs, may be due to a difference of strains collected in a widely separated geographical area.

Among the several conclusions is one of considerable interest, "The order of importance of transmission by fleas is the following (a) By the blocked flea serving as a biological vector (b) Mechanical transmission which undoubtedly is of considerable importance during an epizootic (c) By the infected flea or its faeces being scratched into the skin (d) By the ingestion of fleas harbouring plague bacilli. Infection by the latter two methods is undoubtedly rare and of minor importance."

W I Harvey

HOPKINS, G H E. Annotated and Illustrated Keys to the Known Fleas of East Africa. Reprinted from *Uganda J* 1947, Sept, v 11, No 2 (Scientific Suppl.), 133-90, 146 figs on 21 pls [35 refs]

The species of fleas dealt with in this paper are those occurring in Kenya, Tanganyika, Uganda and Zanzibar. Rather less is known about the fleas of Tanganyika than of those of the other territories. With the exception of the common poultry flea (*Echidnophaga gallinacea*), there seems to be an absence of indigenous bird fleas in spite of the fact that many nests have been examined.

The worker is urged, when using the keys, to have his provisional identifications checked by a specialist except in the case of the commonest fleas. Most of the characters used for identification are shown in a diagram and the important morphological details for distinguishing species are figured. In addition to the keys, there are notes on characters for separating closely related forms, on bionomics, the technique of collecting, preparation for study, preserving and on control. The index contains the names of 25 genera and over 80 names of species and subspecies.

H S Leeson

MCDougALL, W A. An Investigation of the Rat Pest Problem in Queensland Canefields. 5 Populations. *Queensland J Agric Sci* 1946, Dec, v 3, No 4, 157-237, 10 figs (1 map), & 3 pls [41 refs]

This monograph, the fifth of a series, is concerned largely with the trapping of rats, especially *Rattus conatus*, in estimating rat populations. It is largely of agricultural interest, but in discussing the influence of disease on population fluctuation in rats, the author notes that bubonic plague in Queensland in 1921-22 did not appear to have any effect on cane rat population trends at

The present study deals with the employment of the same treatment in a certain number of cases of dengue in East Africa, with similar happy results. Five charts are reproduced showing in each case a rapid fall of the temperature.

[Although the relief of symptoms by decompression is not surprising the complete arrest of the febrile process in a virus disease is truly remarkable. In view of the wide range of variation that is known to occur in the duration and severity of attacks of dengue, a fully controlled test of the treatment ought to be carried out. The author describes dengue as a fever lasting eight to nine days with two paroxysms of fever unbearable headache, and invariably followed by a long period of weakness and depression but short "one-phase" attacks and rapid recovery are common in certain outbreaks.]

John W. D. McGee

### PLAGUE

BURROUGHS, A. L. *Sylvatic Plague Studies. The Vector Efficiency of Nine Species of Fleas compared with *Xenopsylla cheopis*. J Hygiene 1947 Aug., v 45 No. 3 371-68, 3 figs. on 2 pls. [59 refs.]*

This study which has sylvatic plague as its background, is primarily concerned with an expression of the vector efficiency of the flea *Xenopsylla cheopis* is used as the basis of comparison. This flea and the domestic rodents, and not the wild rodent reservoir are considered to be the agents responsible for bringing plague into contact with human beings. The fleas studied were — *X. cheopis* *Draconus montanus* *P. irritans* *Oropsylla idahoensis* *Neopsyllus fasciatus* *Echidnophaga gallinacea* *Orchopeas saxatilis* *sericeolatus* *Opiodarys nesiotes* *Megabothris ebneri* *Malaricus telchium* and their hosts are noted.

In the United States, up to the present, only 66 cases of plague infection in man have been traced to sylvatic rodents. In the present paper in addition to the main subject matter that of numerical expression of vector efficiency there is a well-balanced historical recapitulation of our knowledge of plague bionomics. Much of this is based on the valuable accounts and documentation of the Indian Plague Research Commission. [It may be well to recollect that there was an earlier British Commission, a Royal Commission 1898-99 of which the medical members were Sir Thos. Fraser, Sir Almoth Wright and Armand Ruffier.]

A great deal of preliminary work on the rat and rat flea was done before the main plague Commission got to work. References are made in the present communication to the experimental establishment of the fact of mass transmission experiments from rat to rat by fleas (Simond, 1889) to Liston's work on the relationship between rat fleas and man (the first public communication of which is recorded in the *Transactions of the Bombay Medical and Physical Society* February 1903) and, possibly more dramatic, the demonstration in 1903 of plague bacilli in the proventriculus of the rat flea fed on infective blood to the conclusion of the Plague Commission (1906) that transmission of infection by a single flea was only remotely possible. Many other facts of the history of plague are brought to mind in the article, such as the comparison of the efficiency of *X. cheopis* and *X. astia* the check on the advance of an epidemic when the mean daily temperature attains 80°F if accompanied by a saturation deficiency (Brooks 1917) of over 0.3 m. that classical work, the first demonstration by Bacot and Martin (1914) of proventricular block by plague bacilli in the rat flea the distinction between pestiferous and pestiliferous fleas, and so on.

We may leave this interesting historical account and proceed to the subject matter proper. WHEELER & DOUGLAS [this Bulletin 1946 v 43, 35] presented an experimental method of measuring numerically the vector efficiency of a flea

species in terms of infection potential vector potential and transmission potential. According to Burroughs the vector efficiency thus obtained represents an approximation to natural efficiency and he points out that this is inevitable because ignorance of ecology precludes the duplication of natural conditions. He uses the well-known statistical formula  $\bar{X} \pm K\alpha\sqrt{\frac{S^2}{N}}$  in order to find the range within which the true value probably lies, "to estimate the expected number of mice killed (total number of daily transmissions) per flea where  $\bar{X}$  is the average number of transmissions per flea for the entire number of fleas studied,  $N$  the total number of fleas used in the studies" and  $\alpha$  'the probability that the estimating interval covers the true value'. In this way, it was found that the true vector efficiency, with a confidence of 90 per cent, of important fleas could be given as — *Nosopsylla cheopis*  $0.660 \pm 0.234$ , *Nosopsyllus fuscatus*  $0.213 \pm 0.157$ , *Orchopeas sexdentatus sexdentatus*  $0.170 \pm 0.138$ , *Diamanus montanus*  $0.02 \pm 0.02$ . The low value and inefficiency given to this last flea, which is grouped with *Opisodysus nesiutus*, *Megabothris abantis* and *Malaraeus telchinum*, is not supported by the work of WIEFLER and DOUGLAS [loc cit] who regard it as an exceptionally good vector ( $0.840 \pm 0.232$ ) and more efficient than *N. cheopis*. This, it is suggested by Burroughs, may be due to a difference of strains collected in a widely separated geographical area.

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W. F. Huxley

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H. S. Lleson

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the time and that *Leptospira sclerochaemorrhagiae* was shown to be non-pathogenic to *R. conatus* from canefields. It is concluded that weather is the prime factor governing survival and fluctuations.

H J O'D Burke-Gaffney

WAGLE, P. M. & COLAH, R. B. M. Prognostic Significance of Leucocyte Count in Baboon Plague. *Indian Med. Gaz.* 1947 July v 82, No. 7 399-402, 1 chart.

There were 446 cases of baboon plague treated with sulphonamides, and analysis was made of the leucocytic reaction and its correlation with both septicaemia and death rate. All those suspected of showing the hyper or hypo-leucocytosis of toxic sulphonamide action were excluded from the series. Where more than one count was made on a patient, the highest result was used for the calculations. If a total count of 5,000 to 10,000 leucocytes per cmm. be taken as more or less normal level the curious fact emerged that this proved to be an optimum condition for prognosis—17.7 per cent. mortality for 79 cases. Three of 6 patients with a count of less than 5,000 died, and mortality in the opposite direction mounted steadily to 97.3 per cent. for a count of over 40,000. The authors think that the counts below the normal base level indicate lack of resistance, and above that level, the degree of reaction was highly correlated with degree of septicaemia. At the same time, septicaemia occurring with a normal leucocyte count was of grave prognosis and was, in fact, a manifestation of lack of resistance. The degree of septicaemia, which is the main factor determining the severity of plague infection, was determined by colony counts of drawn blood sown on agar slopes. Mortality rates of the 446 cases worked out at 7 per cent. for the non-septicaemic, 54.9 per cent. for the septicaemic, 21.8 per cent. for the mild septicaemic and 63.8 per cent. in severe cases.

W F Harvey

## AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

✓ ALKAN W Amoebiasis as seen during 18 Months with a Military Hospital, Harefah, Jerusalem. 1947 Nov 2, v 33 No. 9 [In Hebrew 143-6 (13 refs.) English summary 148.]

The author describes 66 cases of amoebiasis seen in 18 months among 4,995 patients, mostly Indians in hospital in Greece and Italy. Dysenteric hepatic and cutaneous forms and the carrier state are reviewed. Many cases were easily mistaken for simple intestinal conditions. Cysts were found in only 14 cases. The author advocates reasonable treatment of every patient infested with *E. histolytica* owing to the inherent danger of apparently inconspicuous infections, the absence of a sharp demarcation between infestation and infection and the apparent general increase in amoebiasis. All the usual diagnostic methods are recommended but treatment, on the whole, was not found to be quite satisfactory. The author finds emetine to be useful only in combating acute symptoms, but it was of value in the treatment of extra-intestinal complications. For the dysenteric form, the other recognized drugs are recommended. The psychological factor in treatment is of importance whatever form of treatment is adopted, relapses are common.

H J O'D Burke-Gaffney



CALVÓ FONSECA, R. La incidencia de la *E histolytica* en Cuba [The Incidence of *Entamoeba histolytica* Infection in Cuba] Kuba Habana. 1947, Oct, v 3, No 10, 220-24

The author reviews the findings which have been recorded by various investigators into the prevalence of infection by *E histolytica* in Cuba. As a result of examination of 38,091 specimens of faeces from persons in 6 Provinces and 126 Municipalities, the general incidence was found to be 2.2 per cent, with lower and upper limits of 0.31 and 6.74 per cent. Going into the question more thoroughly, the author studied the reports from various countries of South America and found that the methods employed varied widely, some examined one slide only, others more, some after a saline purge had been given, others not—in short, there was no uniformity and the results were, in consequence, not really comparable.

The author, therefore, proposed, and the Section of the Medical Congress held in December, 1946, supported, the resolution, that some standard should be adhered to, and four points were decided upon: (1) That the number of specimens should be more than one, if the first proved negative, and that, under these conditions, examination should be made after administration of a saline purge. (2) That the number of persons examined should be at least 2 per cent (better 5 per cent) of the population. (3) That, whether urban or rural, a fair cross-section of the social groups should be included and, for this purpose and to include both sexes, those attending school between the ages of 6 and 18 years would be best. (4) Method of examination: (i) The preparation should be a thin one, with physiological saline as diluent, (ii) another preparation should be examined, diluted with Lugol's iodine, (iii) a Gram-stained preparation for searching for protozoa and cysts should be made, (iv) a specimen should be examined by Faust's concentration method, as modified by OTTO, HEWITT and STRAHAN [this *Bulletin*, 1941, v 38, 473].

[This method may not find recommendation from all, but there is much to be said for some standard procedure in order that results reported by investigators in different countries can be compared.]

H Harold Scott

CONVERS, F. El examen radiológico en los abscesos amibianos del hígado [Radiology in (Diagnosis of) Amoebic Abscess of the Liver] *Rev Facul de Med* Bogota 1947, June, v 15, No 12, 727-53, 31 figs

An interesting series of X-ray photographs showing the presence of liver abscess, with notes on each of eleven cases out of 50 which the author has had under his observation and care in Colombia. In all, the right lobe was involved, in many cases the X-rays established a suspected diagnosis, in others they revealed an abscess when there had been no suspicion of such. Injection of air, after puncture, the author found very useful in defining the limits of the abscesses. Eight of the cases noted were treated by puncture and administration of emetine, the other three showed enlargement of the liver, but in one only a small collection of pus, and the condition cleared up after administration of emetine, without operation.

H Harold Scott

MORTON, T. C. & SOUTAR, S. F. Amoebic Abscess of the Left Buttock in a Symptomless Cyst Carrier *Brit Med J* 1947, Dec 20, 996-7

A case of amoebic ulceration of the buttock in a symptomless cyst-carrier is described. The patient had previously been kicked on the same area during a football match so that there had been a local injury. About one and a half years later, a fluctuating swelling appeared containing pus infected with

heterophyid adult flukes in the feces of the same patient after a routine chenopodium treatment clinches this important finding. The patient died a year after of vascular accident resulting from the rupture of esophageal varices. Scrapings of the small intestines still showed heterophyid flukes thus confirming definitely our previous findings.

VON BOMENDORFF B. The Site of Infestation with Fish Tapeworm determined by means of Intestinal Intubation. *Diphyllobothrium latum* and Pernicious Anemia. *A Acta Med Scandinavica*. 1947 Nov 25 v 129 No. 3 213-33 9 figs. [10 refs.]

The author has recently discussed the question of localization of *Diphyllobothrium latum* in the human intestine, as a result of information amassed in replies to a questionnaire [see this *Bulletin* 1948, v 45 198].

He has now carried the matter a stage further by attempting to determine the point at which eggs or proglottides might be found by means of intestinal intubation and aspiration of intestinal contents.

The method employed is described and should be studied in the original; it consisted of a modified duodenal tube. It has certain disadvantages, which are discussed. The tests were made on tapeworm-carriers with and without pernicious tapeworm anaemia and comprised 28 persons. 10 had a normal blood picture, 3 had "non-pernicious" anaemia, 10 had manifest pernicious tapeworm anaemia, and 5 had the last named condition in spontaneous remission.

The results are shown in a table in the text and full blood and clinical details are given in three other tables. From these, it can be seen that where pernicious T.A. was present the worm was in the jejunum (95-135 cm. from the mouth) while in non-anaemic persons, those with non-pernicious anaemia and those with remissions of pernicious T.A. the worm was not found before the ileum was reached (up to 334 cm.). It is suggested that when the worm is high up in the intestine, it has an opportunity of impairing the interaction between Castle's extrinsic and intrinsic factors, thus causing a pernicious anaemia [see this *Bulletin* 1947 v 44 1081]. H. J. O. D. Burke-Gaffney

HIRVONEN M. On the Differential Diagnosis between Pernicious Tapeworm Anemia and Cryptogenetic Pernicious Anemia in Carriers of *Diphyllobothrium latum*. *Ann. Med. Intern. Fenniae* 1947 v 36, Suppl. 2 30 pp. 29 figs.

The object of the work discussed in this careful and detailed monograph was to help in establishing the differential diagnosis between pernicious anaemia (P.A.) and severe tapeworm anaemia (T.A.) in carriers of *Diphyllobothrium latum*. The question is of special importance in Finland where *D. latum* infection is common and an unjustified diagnosis of pernicious anaemia may involve a patient in a long, anxious and expensive course of unnecessary liver treatment, perhaps for the rest of his life.

The author establishes this differential diagnosis on the basis, firstly, of examining for free hydrochloric acid in the gastric juice: its presence eliminates a diagnosis of P.A. but its absence does not necessarily help the diagnosis. The patient is then given worm cure as a first stage if he can stand it, but if his Hb. percentage is below 25 and his red corpuscles below 1½ million per cmm., this may prove to be dangerous unless liver treatment is first administered, and in fact such a measure had a fatal result in two of the cases described. After the worm cure, blood regeneration should be studied microscopically: if the blood picture becomes normal on worm cure alone, the case

is one of T.A., and may be so even if this regeneration ceases and only begins again after liver treatment. The pathology of this latter state is discussed and it is suggested that it may be an intermediary stage between T.A. and P.A. In doubtful cases, the differential diagnosis can only be established by prolonged re-examinations after liver treatment and apparent regeneration of the blood picture. If, on the other hand, the patient's blood state is too low or for other reasons he is too weak to have worm treatment as the first therapeutic measure, and no free HCl is present in the gastric juice, these same prolonged re-examinations are required. Finally, the author makes the important differential point that P.A. hardly ever appears before middle or old age.

The material for these investigations consisted of 34 cases of severe anaemia in *D. latum* infections. These are divided into 3 main groups: (1) the certain T.A., (2) the differentially uncertain, and (3) the certain P.A.

In group (1) there were 12 patients with free gastric HCl, although in three, and probably four, liver treatment was required in addition to worm cure before blood regeneration became complete. In this group were also 7 patients with no free gastric HCl who nevertheless recovered completely on worm cure alone.

In group (2) there were 5 patients without free gastric HCl who received liver treatment, but whose improvement was maintained even after this treatment was stopped. There were also 6 patients in whom the diagnosis was uncertain because after-examination was not practicable (in two cases, cited above, owing to death).

In group (3) there were 4 certain cases of cryptogenic P.A. all occurred in old people and continued liver therapy was necessary. The author considers that the removal of the worm was a side-issue in their treatment.

H. J. O'D. Burke-Gaffney

MAZZOTTI, L., RODRIGUEZ, L. & TREVIÑO, A. Observaciones en 161 personas parasitadas con *Taenia* [Remarks on 161 Cases of Taeniasis]. *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico 1947, June, v 8, No 2, 155-62. English summary (8 lines).

The authors, during the past three years, have had under observation 161 persons infested with *Taenia*, 141 with *T. saginata* alone, 16 with *T. solium* alone, and 4 with both species. One hundred and thirty received treatment, 15 of those with *T. solium*, all four of those with both infestations and 111 with *T. saginata* only. Most of the patients were in the third decade; the youngest was a girl of 2 years and the oldest was aged 70. In 10 of the *T. solium* cases, eggs were found in perianal smears and in 4 others on the body and on the underclothing. Ninety-five of the patients complained of "nervous disturbances," change of character, irritability, nausea and, rarely, paraesthesiae; 38 suffered from pruritus ani, 29 from abdominal pain.

Three forms of treatment were given, but, as preliminary to all, the patient was put on a semi-solid diet of cereals, gruel, eggs, soft fruits, etc. on the day before, a saline laxative the same evening, a warm water enema the next morning and, before any food was taken, the specific medicament, divided into three doses, was given at half-hour intervals and, 1½ hours later, a saline purge. The patients were divided into three groups. Group I, 59 patients, received ethereal extract of male fern. In 22 the scolex was found, in 37 it was not, but 4 of these did not relapse; this is regarded as a 44 per cent cure. A second group of 52 was given the oleoresin of male fern, 2-3.5 gm. to adults, 15 cgm. for each year of age to children, in three doses as before, in gelatin capsules. In 42 (80.7 per cent) the scolex was recovered. A third group of

19 were given pumpkin seeds. 300 gm. was the total dose, but as this was so large an extract was made with sulphuric ether to remove fats and a watery extract made of the residue, the total dose being 125 cc. In three the scolex was recovered, from 16 it was not, but 7 of the latter did not relapse, the result being reported as 53 per cent. cura. The fact of the ova of *T. solium* being found on the body and underclothes may explain some of the cases of human cysticercosis.

H. Harold Scott

HOOD M. The Present Status of Hookworm Infection in Florida. *Amer J Trop Med* 1947 July v 27 No. 4 505-16 3 charts & 1 fig. [16 refs.]

The importance of hookworm infection as a medical problem in Florida was recognized in 1903. Hookworm campaigns and surveys have been repeatedly undertaken since that date. The first survey undertaken under the auspices of the Rockefeller Foundation in 1910 showed that 58.1 per cent. of 6153 persons examined had hookworm infection. In 1926, another survey showed a 56.2 per cent. infection rate. It was at one time assumed that infection and disease were synonymous, but later by employing counting methods, SMILLIE and AUGUSTINE [this Bulletin 1928 v 23 772] showed that only heavy (12,600 and over eggs per ml.) and moderately heavy (2,600-12,599) infections were clinically significant. Persons with light (700-2,599) and very light (200-699) infections did not improve in health significantly after anthelmintic treatment, while those with heavy infections did. A third survey, in 1937-38 undertaken by a Vanderbilt group [ibid 1939 v 36 823], showed a 34.8 per cent. infection of 29,064 specimens of those 11.5 per cent. were classed as moderate or heavy infections.

For the present survey the zinc sulphate concentration method was used to detect infections and also for estimating intensity. Parallel egg counts by the Stoll and zinc sulphate techniques were made in order to establish a ratio, as it was shown that 1 to 40 eggs per cover-glass constituted a very light infection, 41 to 150 a light, 151 to 700 a moderate, and 701 and over heavy infection.

A study of 8,017 white school children showed a marked variation between the counties in both incidence and intensity of infection. Approximately 40 per cent. of the white children have hookworm infection but only 3.9 per cent. of the whole number or 10 per cent. of the positive cases, are classed in the moderate and heavy intensity groups.

Very low incidence and intensity of hookworm infection are shown in a group of 1,264 coloured children studied (13.3 per cent. positive).

Hookworm infection is most marked during school age. A sharp diminution in both incidence and intensity is shown about the twentieth year.

Both incidence and intensity of hookworm infection are greater in the western section than in any other area of the State.

It is considered that, although there has obviously been a great reduction in the hookworm incidence in Florida, it is still a public health problem. It is believed that better results will be obtained in anti-hookworm campaigns if all infections are reported according to their intensity so that efforts can be concentrated on groups that show the largest number of moderate and heavy infections.

L. E. Napier

HERNÁNDEZ LIRA, J. P. Aspecto mexicano en relación con la clínica y el tratamiento de la uncinariasis. [Ankylostomiasis in Mexico.] *Medicina*. Mexico. 1947 Nov 10 v 27 No. 543 481-83.

After general remarks on the history of ankylostomiasis and its symptomatology the author speaks in detail of the methods of treatment used in Mexico.

He mentions various drugs which have been tried from time to time and states that several "accidents" have occurred after administration of oil of chenopodium and of carbon tetrachloride, and in consequence the latter has been discarded altogether, and at the present time only three drugs are used, namely, oil of chenopodium (with 76 per cent ascaridole) hexylresorcinol, and tetrachlorethylene. The first is specially serviceable because *Ascaris* infestation often accompanies that with hookworm. To children of 3-4 years of age 0.1 cc is given, of 5-6 years 0.15 cc, and 7-8 years 0.20 cc, with a purge of castor oil. To those above this age the drug is given in capsules (dosage is graded, adults of 20 years or over receiving 1.25 cc) and a saline purge is given one hour later. Patients are examined before treatment is given to find out if there are any contraindications. The drug is given before any food is taken and the patient is kept under observation for 2-3 hours for any signs of absorption. *Hexylresorcinol* is given as chocolate-coated pills of 0.2 gm each, in doses of 0.07 gm per year of age, so children of 6 years are given two pills, or 0.4 gm, of 6-8 years three pills, 8-12 years four pills, and those over 12 years five pills or 1.0 gm. No food is allowed for four hours afterwards and a saline purge is usually given. Tetrachlorethylene [the formula is wrongly given as  $Cl_2C_4$ , instead of  $C_2Cl_4$ ] is administered to adults in amounts of 2 cc in divided doses (3 cc may be given to powerful adults without harm and proportional doses to younger subjects) followed by a purge of sodium sulphate. If ova were found a week later the dose was repeated. Of 458 patients so treated, 11 per cent were cured after one treatment, 16 per cent after two, 27 per cent after three, 40 per cent after four and 98 per cent after five treatments. In all cases, the patients are kept under observation and the anaemia consequent on the infestation is treated with iron preparations.

H Harold Scott

GUEVARA, R. Toxicity of Oil of Chenopodium when administered together with Castor Oil. *J Philippine Med Ass* 1947, June, v 23, No 6, 259-67 [15 refs]

Oil of chenopodium is a well-recognized anthelmintic. Its active principle is ascaridol, and it is used in the treatment of *Ascaris* and hookworm infections. In ordinary doses it paralyzes but does not kill the worms, it is therefore necessary to follow the administration of this drug by a purgative. It is convenient to give this purgative at the same time as the drug. Castor oil is often used as the purgative. The combined administration is usually looked upon as a safe procedure, but in the Philippines a prejudice has arisen against giving castor oil with oil of chenopodium. It is thought that this is because a popular mixture containing oil of chenopodium and castor oil has given rise to toxic symptoms and in some cases death. There are, however, other ingredients in this mixture.

An investigation was undertaken to prove or disprove the theory that castor oil increases the toxicity of oil of chenopodium. Cats, twenty-seven in all, were used as experimental animals. With a dose of oil of chenopodium of 0.20 ml per kilogramme, all the cats died, with a dose of 0.1 ml all survived, and with a dose of 0.15 ml one died and two survived. When 15 ml of castor oil was added to each dose of oil of chenopodium, all cats survived doses up to 0.30 ml, one out of three survived 0.35 ml and all three died with doses of 0.40.

The author concludes that the addition of castor oil halves the toxicity of oil of chenopodium rather than increases it, and that, as there are more advantages in taking the combined drugs than each drug separately, this procedure should always be followed.

The symptoms of toxicity were vomiting, general muscular weakness, prostration, ataxic convulsions, stupor coma and death, convulsions being the most prominent and lasting several days prior to death. L. E. A. *post*

GUTMAN F & MORALEZ, P. Ascaris in the Cansian BBe Duet. (A Report of 10 Cases) *J Philippine Med. Ass.* 1946, July v 22, No. 7 289-303.

GALLIARD H. Evolution de *Wuchereria bancrofti* et *W. malayi* chez *Aedes* (*Stegomyia*) *aegypti* et *A. (S.) albopictus*. [Development of *Wuchereria bancrofti* and *W. malayi* in *Aedes aegypti* and *Aedes albopictus*.] *Ann. Parasit. Humains et Comparée.* 1947 v 22, No. 1/2 30-35.

Complete development of *Wuchereria bancrofti* in *Aedes aegypti* was demonstrated in certain cases, while in others the development was partial only or abortive. Early larval stages only were found in *Aedes albopictus*.

Complete development of *W. malayi* was observed in a small percentage of cases in both species of mosquitoes. J J C Buckley

ROGERS, L. The Present Position of Antimony Treatment of Filariasis: with a Suggestion for its Intensive Use. *Indian Med. Gaz.* 1947 June, v 82, No. 6 348-8.

Recent work in filariasis at Porto Rico confirms the author's observations made in 1919-1920 regarding the effect of antimony in this infection.

After Christopherson's observations on the effect of sodium antimonyl tartrate in schistosomiasis the author carried out preliminary investigations at Pura and later at Caticlat jail. In the latter investigation, eight persons with high microfilaria counts average 73 per 20 cm. [200 mm.] were chosen and treated with sodium antimonyl tartrate with doses up to 5 ml. of a 2 per cent. solution intravenously. In four cases, the microfilaria counts fell steadily for 3 months after the cessation of treatment, reaching 3 to 9 per cent. of their original number whereas in four others after an early fall in the counts, every month there was a sharp rise which brought the microfilaria curve back to the original level. These peaks were due to the sudden appearance of young embryos, easily distinguished from older forms. The author concluded that, in the first four cases, the adult worms had been killed or very seriously damaged.

These observations were confirmed by DAS in India [1920] DAY in Egypt [Lancet 1921 Mar 12, 525] ROY & BOSE [Indian Med. Gaz. 1922, v 57 231] and BAR in the Dutch East Indies [no reference]. These workers also showed that the repeated attacks of febrile lymphangitis were eliminated or reduced in frequency and that in cases of elephantiasis there was a reduction in the diameter of the limbs after 2 to 5 doses of sodium antimonyl tartrate. These observations were not confirmed by the British Guiana Filariasis Commission under LIPER [Lipier].

In 1943 Professor Culbertson of New York [CULBERTSON ROSE & OLIVER-GONZALEZ, this Bulletin 1946 v 43 354] showed that antimony killed the adult filariae in the pleural cavity of cotton rats, but that the microfilariae continued to circulate in the blood for many months and that the drug had a similar effect in man if the cases were followed long enough. Some of their cases were followed for 3 years. The best results were obtained with neostibosan, given in intensive doses up to totals of 15 grammes. With small doses of tartar emetic, average total 0.79 grammes, reductions to 41 to 6 per cent. of the original microfilaria counts were obtained.

The author concludes that neostibosan is the drug of choice, but considers that it may prove too expensive in the endemic areas, and suggests that intensive treatment by sodium antimonyl tartrate as used by ALVES & BLAIR [this *Bulletin*, 1946, v 43, 344] in schistosomiasis, might be as effective in filariasis

L E Napier

RUIZ REYES, F Tratamiento experimental en la oncocercosis con el "Naphuride Sodium" [Naphuride Sodium in the Treatment of Onchocerciasis] *Medicina Mexico* 1947, Oct 25, v 27, No 542, 475-7

[If more investigators had the courage to report negative results, we would hear less of the success of remedies vaunted on one or two beneficial effects] The author, at the request of Dr CULBERTSON of the University of Arkansas, has taken up anew the subject of this drug and its action in onchocerciasis. Naphuride sodium, a product of the Winthrop laboratories, is a synonym of Germanin, Bayer 205, Moranyl, 309 Fournneau and Naganol. The author has tried it in five cases of onchocerciasis of 10-15 years' standing, with abundant embryos in the skin, and two of the patients are blind. Each was given 1 gm in 10 cc of doubly distilled water intravenously once a week for five weeks. The weights of the patients ranged between 38 and 50 kgm, and their ages between 16 and 62 years. The drug caused headache, nausea, vomiting and occasionally "severe nephritis," but early examination of the urine (2 days after each dose) forestalled any untoward effects [so says the author, who evidently does not regard severe nephritis as such an effect]. The results on the infestations were controlled by frequent biopsy examinations of the skin to determine whether the embryos were killed by the drug. A table gives the detailed results of the many biopsies and the only conclusion which can be drawn is that "Naphuride Sodium has no obvious effect on onchocerciasis when given by the method described in this article"

H Harold Scott

BERTRAM, D S The Period required by *Litomosoides carini* to reach the Infective Stage in *Liponyssus bacoti*, and the Duration of the Mites' Infectivity *Ann Trop Med & Parasit* 1947, Sept, v 41, No 2, 253-61

Three series of mites were infected and maintained on cotton rats and on white rats by methods previously described. By these methods, the date on which the mites first become infected is known within a limit of twenty-four hours. An account is given of present experiments and the following is the author's summary —

"It is concluded that white rats and cotton rats which become positive for *L. carini* after serving as hosts to infected female *L. bacoti* are infected by the transmission of the active thread-like worm larvae which develop in the mites. Transmission appears to occur in association with the feeding habits of the mite but the actual mode of transmission is not known, and other methods of transmission by the mite cannot be discounted.

"Infected mites stored at 23-25°C and maintained by blood-meals at approximately five-day intervals first transmit the infection of *L. carini* to white rat and cotton rat hosts on the occasion of the third meal, or the 15th day, after the mites' infecting meal. Transmission continues until the fifth meal on the 25th day, possibly with diminishing intensity, and it may occur until later than the seventh meal or the 36th day after the mites' infecting meal.

"Of two cotton rats exposed to infection by 17-30 mites of a series in which 38 per cent were positive, one rat which was exposed for 24 hours on the 15th

day after the mites infecting meal developed an infection averaging 278 mf./cmm. of peripheral blood (range 90-670 mf./cmm.) in 20 weekly counts the other rat which was exposed for 24 hours on the 20th day after the mites infecting meal developed an infection averaging over 18 weekly counts, 97 mf./cmm. of peripheral blood (range 40-190 mf./cmm.) A third rat exposed to 3-13 mites of this series on the 25th day of their infection contained only one male *L. carinii*.

Cotton rats were found to be positive for the microfilariae of *L. carinii* in the peripheral blood-stream 51-64 days after a 24-hour period of exposure to infection by infected mites.

Non-infective forms of the worm with sickle-shaped tails occur on the ninth and tenth days of the worm's development, and the infective forms appear to be the active thread-like worms varying between 0.5 mm. and 1 mm. in length found from the 14th day to the 36th day after the mites infecting meal.

The percentage infection-rates in two series of mites dissected before the first infective meal were as follows: 38 per cent. of 29 mites were positive for 1-5 worms after engorgement on a cotton rat showing 2,584 mf./cmm. of peripheral blood. 21.8 per cent. of 39 mites were positive for 1-2 worms after engorgement on the same rat on a separate occasion when the blood count was 3,000 mf./cmm. of peripheral blood.

H. S. LAYTON

## HAEMATOLOGY

BICKEL, G. Hämglobinstandardlösung zur Eichung von Hämglobin nach Sahli od. Zelenko [Haemoglobin Standard Solution for the Sahli and Zelenko Haemoglobinometers.] *Schweiz. med. Woch.* 1947 Dec. 13, v 77 No. 50 1312-13, 1 diagram. [12 refs.]

SCHREYER, G. W. H. Macrocytic Hyperchromic Anaemia on the Witwatersrand. Parts I & II. *South African Med. J.* 1947 Aug 9 & 23 v 21 Nos. 15 & 16, 566-75 605-11 9 figs. [13 refs.]

On the Witwatersrand, approximately 6,000 feet above sea-level, 300 patients with macrocytic or hyperchromic anaemia were discovered. As there was potential reservoir of approximately 50,000 persons the incidence of the anaemia was at least 0.6 per cent. which is considerably in excess of that for pernicious anaemia. A survey suggested that on the Witwatersrand, probably because of the altitude, 5.5 million erythrocytes per cmm. for men and 5 million for women, with corresponding increases in haemoglobin values, should be taken as minimum requirements. Observation showed that the haemoglobin concentration increases as the cell count, but that the rate of increase shows a diphasic, or perhaps tri-phasic trend. Thus for cell counts between 4 and 5 million per cmm. the rise in haemoglobin is very steep but above and below these limits the curve shows deceleration which is progressive as the lower and upper limits are approached. Similarly it was found that as the cell counts varied from 5 to 3 millions per cmm. the mean cell diameters increased from approximately 8.0 microns to about 10.0 microns, but beyond these limits in either direction the rate of change in cell volume was less than that of the cell count. A curve obtained by plotting the colour index against the mean erythrocyte surface showed no diphasic character the colour index increasing with increase of cell surface area up to the normal mean of 75 square microns per cell although beyond this the curve showed an increasing deceleration. In the macrocytic anaemias the concentration of haemoglobin per unit





## VENOMS AND ANTIVENENES

GRASSET E. & CHRISTENSEN P. A. Enzyme-Purification of Polyvalent Antivenene against Southern and Equatorial African Colubrine and Viperine Venoms. *Trans. Roy. Soc. Trop. Med. & Hyg.* 1947 Oct. v 41 No. 2, 207-11

Enzyme-purification of polyvalent South African *Vaje flavo-Bitis ardens* antivenene, and polyvalent *Bitis gabonica* antivenene resulted in from four to six times concentration, and an increase in nitrogen content to approximately double the original amount. Group neutralising antibodies against other African colubrine venoms, namely *V melanoleuca* *V kaje* *N nigricollis* *Sepedon haemachades* and *Dendroaspis angusticeps* were concentrated to useful therapeutic levels. Limited protection was observed against the venom of *Bitis marcoris*. The speed of union between enzyme-treated antivenene and venom is high.

The increased antibody concentration and purity of enzyme-treated antivenene marks a big therapeutic advance in the treatment of snake-bite, as compared with the antivenene previously prepared by fractional sodium sulphate precipitation, and its use reduces the risk of serum reactions.

EICHBAUM, F. W. A Diffusion-Precipitation in the Titration of Antivenins (Antibiotropic Sera). *J. Immunology* 1947 Oct. v 57 No. 2, 101-14 6 graphs.

## DERMATOLOGY AND FUNGUS DISEASES

WILLIAMS, W. The Tropical Lichen Planus Syndrome. *Brit. Med. J.* 1947 Dec. 8, 801-4 2 figs.

The author describes in detail three cases, and discusses a possible fourth case of this condition, the incidence of which was estimated at 1/2,000 troops. All were members of a New Zealand force operating in the Solomon Islands, a highly malarious region where suppressive mepacrine was administered to all troops at a rate of 0.1 gm daily for six days in each week.

The patients—two white soldiers and a quarter-caste Maori, had been taking suppressive mepacrine for eight to twelve weeks before the first symptoms developed and in all cases it was noted that fresh lesions appeared while mepacrine was being taken but ceased soon after its discontinuance.

The disease began as a patchy hyperkeratosis of the palms and soles, accompanied by thickening of the finger and toe nails which became brittle and opaque. Later a rash developed on the trunk and limbs which consisted in two cases of pink macules  $\frac{1}{2}$  to  $\frac{3}{4}$  inch in diameter, and in the third of raised bluish purple areas some of which were an inch in diameter. In two cases, lesions suggestive of syphilitic mucous patches developed on the buccal mucosa.

As the disease progressed scaling occurred on the individual lesions and variable degree of follicular hyperkeratosis developed on the back and shoulders.

The disease took a course of six to twelve months during which the thickened skin of the palms and soles was shed, and pigmentation occurred on the original patches. In some areas, vitiligo replaced the original pigmentation, and this variegated pattern appeared to be permanent. There was marked atrophy of the skin at the site of some of the healed lesions. Throughout the course of the disease the general health remained good. No evidence of spirochaetal or mycotic infection was found in any case nor was the author able to transmit the disease by inoculation of a volunteer with serum from scarified lesions.

The cases were therefore regarded as examples of tropical lichen planus, a condition which appears to be related to the use of mepacrine as a malaria suppressive  
H T H Wilson

KULOWSKI, J & STOVALL S Maduramycosis of Tibia in a Native American J Amer Med Ass 1947 Oct 18 v 135, No 7, 429-32, 3 figs [Refs in footnotes]

CALERO, C Cromoblastomycosis Acción *in vitro* de las sulfas sobre tres razas fungosas encontradas en el Istmo de Panama [Action *in vitro* of Sulphonamides on Three Strains of *Fonsecaea pedrosoi* in the Isthmus of Panama] Rev Inst Salubridad y Enfermedades Trop Mexico 1947, June, v 8, No 2, 119-23

The English summary appended to the paper is as follows —

"In accordance with our observations 'in vitro,' in regard to the effects of four sulphonamides on the growth of three Panamanian strains of *Fonsecaea pedrosoi*, the sulphapyridine seems to produce the most notable inhibitory effects

"Our observations also seem to indicate that these drugs have a certain inhibitory effect on the sporulation of fungi studied, the effect particularly notable on phialophoric type of sporulation less effective on acrotheca sporulation, and much less notable on hormodendrum type of sporulation

"The study 'in vitro' on the four kinds of sulphonamides used in the growth of the three pathogenic strains of *Fonsecaea pedrosoi* (Brumpt) Negroni, 1936, encountered on the Isthmus of Panama, ratifies the observation 'in vitro' already reported by Pardo Castelló *et al* (1942)"

FORBUS, W D & BESTEBREURTJE, Annie M Coccidioidomycosis a Study of 95 Cases of the Disseminated Type with special reference to the Pathogenesis of the Disease Milit Surgeon 1946, Nov, v 99, No 5, 653-719, 37 figs (4 coloured) [236 refs]

This long and masterly description of the clinical and pathological features of coccidioidomycosis, which should be read in the original, is based on the study of materials obtained by biopsy and by necropsy from 95 cases of the disease in its disseminated form, supported by the clinical and pathological records

Following the method used in the classification of pulmonary tuberculosis, the authors distinguish two stages of coccidioidomycosis, (1) a primary complex which may be symptomatic or asymptomatic, and (2) an endogenous reinfection leading to disseminated disease. Hitherto, little was known of the pathology of the primary, pulmonary stage of coccidioidomycosis, in which death rarely occurs, but the authors "have been able to construct, according to well-established pathologic principles, the probable pulmonary reactions to the primary infection with *Coccidioides immitis*" and they recognize four forms of the pulmonary lesion (a) Lobular, focal, pulmonary consolidation strongly resembling the ordinary type of bacterial pneumonia, (b) extensive, gelatinous, focal or confluent, or lobular consolidation, (c) necrotizing, ulcerative bronchitis and bronchiolitis with bronchiectasis and bronchiectatic cavity formation, and (d) focal lobular or massive lobar, indurated, grey, moist, granulomatous consolidation. In its milder forms, the primary disease usually resolves without leaving any permanent change in the lung tissue, but the suppurative and the granulomatous, necrotizing lesions heal with scar formation. It is noteworthy that the authors found calcification of these lesions

this type of heat-exhaustion was due to local causes. Australian Army physicians described a similar syndrome in which, by means of serial sections of skin, they found blocking of the superficial parts of the sweat ducts and cystic dilatation of the ducts beneath the block. Polyuria was marked in this syndrome. Heat-exhaustion type 2 does not endanger life: no case developed into heat-stroke. Yet it was of military importance, because the incidence was high and the rate of recovery slow.

ii. Work done by the Heat Physiology Team at the National Hospital, London, on the effects of high temperatures on man is described by Ladell. With acclimatization to heat sweating starts at a lower rectal temperature, and later reaches a higher rate for a given rectal temperature. At the same time the cardiovascular system becomes adjusted, probably because of an increase in the plasma-volume. Men are apparently physically efficient, and able to continue work for periods up to two hours, with rectal temperatures of 102°F., but in the light of observation and personal experience 101°F. was taken as the acceptable upper limit. The sweat glands appear to become fatigued rapidly at high rates of secretion. The decline of sweating after a certain length of time occurs whether the subject is replacing his water (and salt) losses or not.

The points considered in deciding whether the given environment should be regarded as tolerable or not were: (i) whether one or more subjects in the group failed to stay the course for four hours; (ii) a final rectal temperature (after work) above 101°F.; (iii) an average sweat-rate over the whole period of more than 1,250 cc. per hour; and a final (after work) pulse-rate of more than 140 per minute. By the use of these criteria, contour lines showing limiting environments were drawn. Of interest and importance is the notable effect of low air speeds. Thus, for men working in shorts, an increase in air speed of from 10 to 25 ft. per min. raised the wet bulb tolerance by 1°F. at high humidities and by 2°F. at low ones. It increased the dry-bulb tolerance by 5°F. and 10°F. at high and low humidities respectively. Increase of air movement from 75 to 200 ft. per min. increased the wet-bulb tolerance by only 1°F. and the dry bulb tolerance by 10°F. at all humidities.

iii. In a further paper Ladell describes an experimental study of the effects on man of restricted water-supply. The work was done on behalf of the Committee for the Care of Shipwrecked Personnel. When little or no water is taken there is a rapid fall in body-weight, because of the cumulative water debt contracted within the body. In a temperate climate a water intake of 800 to 900 cc. per day was needed to maintain water balance. Physical deterioration ran parallel with weight loss. A 5 per cent. loss was tolerable, but with 10 per cent. loss, such as occurred after 60 hours deprivation gross deterioration, physical and mental began to set in. Some constituents of lifeboat rations had diuretic effect and proposals were made for amended rations. Measures for increasing the water supply in lifeboats were explored. Diuresis is caused by the drinking of sea-water but with intakes of less than 400 cc. per day the increase in urine volume is less than the volume of sea-water drunk, so that there is a net gain of water to the body. Higher intakes of sea-water cause a drain on body water: hence larger amounts of sea-water are dangerous. Water requirements are high in the tropics, and water deprivation very quickly causes dehydration. Thirst is a poor index of the need for water and it was recommended that each man should drink enough to produce at least beer-bottle and a half (about 850 cc.) of urine each day.

iv. The effects of a tropical climate on men in warships are discussed by Ellis. A Sub-committee of the Royal Naval Personnel Research Committee recommended that an effective temperature of 80°F. was the upper desirable limit for working and living compartments in ships, while 86°F. was the upper acceptable limit. The average thermal conditions in eleven ships with the

# Tropical Ulcer

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Eastern Fleet in 1944 are tabulated. In each type of compartment listed, the average effective temperature exceeded the upper desirable limit, and in most of them the upper acceptable limit was exceeded. Sickness rates, and causes of sickness, in 28 ships and 6 naval shore establishments are discussed. Prickly heat was very prevalent, and affected 80 to 90 per cent of the men at one time or another. Excluding prickly heat, 9 per cent of the effects of heat on the efficiency of wireless operators, carried out by Mackworth, are summarized. Efficiency declined when the effective temperature was between 83° and 87.5°F, and at higher temperatures observed in wireless and radar offices that the average effective temperatures were about 86° and 87°F, respectively. v Weiner discusses the biological assessment of clothing for use in tropical service. For most military purposes, the thermal study of clothing is reduced to a few easily-measurable criteria—rectal temperature, pulse-rate, sweat output, water regain by clothing, and, where possible, the evaporated and un-evaporated fractions of the sweat-loss of the subject. It is important that subjects shall be fully acclimatized before clothing tests are begun. In examining fabrics for mosquito-proofness, main reliance was placed on a test in which an arm, covered with the fabric, was exposed to the bites of 200 starved *Aedes aegypti*. The number of weals in 15 minutes was noted. The physical characteristics of clothing fabrics relevant to performance in the tropics are the thickness, weight per unit area, water-vapour resistance ("ventility"), air permeability, water absorption and drying-out, and the construction of the cloth. Fabrics for special service garments were studied.

Thomas Bedford

## TROPICAL ULCER

STERNFELD, J & HIRSCH, W. *Ulcer Tropicum*. Clinical and Bacteriological Description of its Epidemic Occurrence in Haifa, 1944. Harefuah Jerusalem 1947, Nov 16 v 33, No 10 [In Hebrew 157-62, 5 figs & 1 graph. English summary 162]

In the first half of 1944, 7 cases of classical tropical ulcer occurred in Haifa among immigrants from the Yemen. In the summer, an epidemic of 122 cases occurred among the local Jewish population. The two forms differed: the ulcers of the Yemenites were typical chronic tropical ulcers of a severe form, and 5 of them showed spirochaetes as well as fusiform organisms. The epidemic ulcers were mild, without general symptoms, easily cured and spirochaetes were found in only 5 of the 122. (Nevertheless, spirochaetes were also absent from 2 of the 7 Yemenite cases.)

Although the presence of spirochaetes seems to increase the virulence of tropical ulcers, the authors believe that it is not necessary to their development. The characteristic microbiological finding is that of fusiform bacteria, with or without other organisms. Severity depends largely on the patients' general health and nutritional state, on clothing and on climate. Up to the present, tropical ulcer has been rare in Palestine and has occurred only in epidemics initiated, it is claimed, by the arrival of Yemenite immigrants, but it is not thought that, even if it became endemic in Palestine, it would acquire the severe character so commonly encountered in the tropics, so long as the conditions for its malignant development do not exist in the local population. [What those conditions are is not indicated in the summary apart from the general factors mentioned above, which are somewhat vague.]

H J O D Burke-Gaffney



THORP, J M & DE MEILLON B Inhibition of the Toxicity of "Gammexane" for Insects [Correspondence] *Nature* 1947 Aug 23 264-5, 1 graph

## REPORTS, SURVEYS AND MISCELLANEOUS PAPERS

ROCKEFELLER FOUNDATION INTERNATIONAL HEALTH DIVISION Annual Report 1946 pp ix+239, 14 figs on 7 pls New York 49 West 49th Street

The report for 1946 maintains the same attractive format, and the same easy and interesting style, as its predecessors. The bulk of work done during the year relates to yellow fever in S America and Africa, malaria studies in relation to chemotherapy, and to control in many parts of the world, influenza and other respiratory diseases, rickettsial diseases, nutritional diseases, virus studies, and syphilis, diphtheria, tuberculosis and certain other subjects. There are also sections dealing with aid to state and local health services, health care, and public health education. At the end is a statement of expenditure each year since 1940, and for the period 1913-1939.

Most of the work published by the members of the staff of the International Health Division has been reviewed in the *Tropical Diseases Bulletin* or the *Bulletin of Hygiene*, but in the short compass of this report the reader will find interesting consecutive accounts of these researches, which will give him a clear idea of their scope.

Charles Wilcocks

## BOOK REVIEWS

HEGH, E [Ingénieur Agronome, Lauréat de l'Institut de France, etc] *Les tsé-tsés Description—biologie—moyens de destruction* [Tsetse Flies their Morphology and Biology and the means of destroying them] 115 pp, 29 figs 1946 Brussels Ministère des Colonies Direction Générale de l'Agriculture et de l'Elevage, Place Royale, 7

This book is a useful introduction to the subject of tsetse flies in general and to those of the Belgian Congo in particular. It admirably suits the requirements of the newcomer to the subject, whether medically interested or not. Where advanced work is referred to in the text and the author lists some of his own publications at the end, otherwise there is no bibliography. There is no from 2 of the ordinary sense, but the table of contents is so comprehensive that although the purpose. Illustrations of tsetse anatomy and of breeding-places tropical ulcers, collected from well-known sources. The characteristic, prising how much the author has managed to get into so little space without other org by explaining the importance of his subject and gives some notes on health and nutriti y of the study of *Glossina* and trypanosomiasis. From this, he tropical ulcer has o describe how tsetse flies may be recognized and distinguished from initiated it is claim. This leads on to descriptions of anatomy and to classification thought that, even il y aspects of bionomics are touched on and their importance is severe character so wh as seasonal movements of the fly, relation to game and domestic conditions for its maligant and feeding habits. Notes are given on the characters of [What those conditions are] species of *Glossina* as found in the Congo, other species are briefly general factors mentioned ok closes with accounts of some natural enemies, parasites and

predators of adult and pupa and with methods of control, including bush-clearing, eradication of game, systematic trapping and the treatment of cattle. Finally there are a few words about the future possibilities of DDT and Gammaxane in the control of *Glossina* when these are applied to animals in the open or in stables, or used in whitewash or in cattle dips.

In the appendices are keys for the identification of tsetse flies in groups of species and as separate species both as adults and as pupae. H. S. Lucas

GELFAND Michael [M.B. (Cape Town) M.R.C.P. Govt. Med. Officer Salisbury Native Hospital, Southern Rhodesia]. *African Medical Handbook. An Outline of Medicine and Hospital Practice for African Nurses, Orderlies and Medical Assistants.* 202 pp. 22 figs. 1947 Cape Town The African Bookman. [15s.]

The fact that another *sales success* for African subordinate medical staff has been produced is a welcome sign of the increasing recognition of the need for adequate training of this class of worker in the Colonies and in Southern Africa.

Unfortunately as the author points out in his preface, there is little uniformity in the designation, status, responsibility and functions of these men and women in the various dependencies. Inevitably therefore, the length and type of training vary according to whether they are destined to serve as nurses, first-aid workers, orderlies, dressers, dispensers, public health inspectors or medical assistants.

It follows that there is a demand for a variety of text books with slightly differing approach and content. This one appears to be a combination of a nurse's manual and a general synopsis. It would appear to be more suited to the nursing orderly for one is constantly reminded that this or that condition or treatment is to be referred to the doctor. There is no section on clinical pathology nor on dispensing both of which would be needed by a worker in charge of a dispensary.

The matter is arranged in 14 chapters, under systematic heads including the topical chapters on Disorders of Nutrition, Tropical Diseases, and Infectious Diseases. The author encounters the usual difficulties in getting things to fit this scheme, e.g. yaws is dealt with under tropical diseases while tetanus is among the infectious diseases. Scabies is raised to the dignity of a tropical disease. A chapter on skin diseases would have been an advantage from many points of view. Salpingitis and ectopic pregnancy are shown under "The Alimentary Tract".

Diagrams are original but not too easy to follow as one must start reading life cycles from the bottom up if one is to work from the known to the unknown, the best tutorial method for backward folk.

Apart from these minor criticisms, the matter is well and clearly set forth in orthodox lines. There are few mistakes ("morbillus" for morbilli being one) and the printing is good. It is a pity that the price has to be 15s. for 200 pages, but the handbook will undoubtedly be popular among those to whom it is intended.

C. C. Chesterman



TROPICAL DISEASES  
BULLETIN

Vol 45]

1948

[No 1

## SUMMARY OF RECENT ABSTRACTS •

## III MALARIA

(Continued from p 228)

## Treatments

A most comprehensive survey of antimalarial drugs has been edited by WISELOCKE (p 1106). It contains a record of the enormous number of compounds tested in the United States during the war. In a series of 6 papers, BRONIE and his colleagues (p 794) have given an account of the methods devised during the war for estimation of basic organic compounds in biological material in connexion with the evaluation of the large numbers of chemotherapeutic agents investigated.

A method of standardization of tests for antimalarial activity of drugs has been devised by GILBERT and SCHUCH (p 970). It is the "quinine equivalent" which is the ratio of the amount of the drug to that of the minimum effective dose of quinine as observed under well defined conditions in *P. cathemerium* infections of canaries.

SHUTE (p 394) points out that strains of malaria parasites vary in virulence and in the amount of antimalarial drug necessary for treatment of the attacks they provoke and that much more of a drug is needed for a primary attack than for a relapse or reinfection.

RAYMOND (p 962) describes the Iotaquin prepared locally in Tanganyika territory during the war. PERRIER GENTIL (p 396) writes favourably of a solution containing quinine gluconate and cilexum for intravenous treatment of *P. vivax* infections. HERTZBLUG (p 26) reports a case of quinine amaurosis in a patient taking therapeutic doses only. SHRAGER and KEVIN (p 170) report a few cases of purpura in both *P. vivax* and *P. falciparum* malaria. This is a serious complication and is apparently an allergic reaction to quinine. No case was found in patients treated with atabrin.

KYKER *et al* (p 802) describe the formation of antimalarial agents by ultraviolet decomposition of quinine. In Holland tablets consisting of quinine and painiquin are used in the treatment of *P. vivax* malaria to prevent relapse (WINKAFL, p 696). MOST *et al* (p 496) is a result of careful observation of a series of patients show that a combined quinine plasmoquine treatment is very much more efficient than

\* The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin* 1947 v 14. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.



# TROPICAL DISEASES BULLETIN

Vol 45]

1948

[No 4

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(Continued from p 228)

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SILVER (p 391) points out that strains of malaria parasites vary in virulence and in the amount of antimalarial drug necessary for treatment of the attacks they provoke and that much more of a drug is needed for a primary attack than for a relapse or reinfection.

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KYKER *et al.* (p 892) describe the formation of antimalarial agents by ultra-violet decomposition of quinine.

In Holland tablets consisting of quinine and pamaquin are used in the treatment of *P. vivax* malaria to prevent relapse (WINKEL, p 696). MOST *et al.* (p 486) as a result of careful observation of a series of patients show that a combined quinine-phosmoquin treatment is very much more efficient than

\* The first list of references with this section of malaria has been compiled is given in the introduction which appeared in the *Tropical Diseases Bulletin* 1947 v. 44. References to the abstracts are given under the names of the authors quoted on the pages on which the abstracts are printed.

McCALL (p. 366) show that sulphadiazine, given for fever with signs of pulmonary disease, delayed the true diagnosis of *P. vivax* infection by eliminating the parasites from the blood, for a time.

TRUFF (p. 485) advocates administration of nicotinic acid, in addition to anti-malarial drugs, in the treatment of severe *P. falciparum* infections basing this treatment on a consideration of the pathology of the disease and the action of the drug.

#### *Suppressive Treatment*

MARGRAITH *et al.* (p. 28) show that mepacrine in whole blood is largely concentrated in the white cell layer but they do not know if it is in the white cells themselves or in the platelets. The red cells and the plasma contain relatively little and the plasma concentration is better than whole-blood concentration, as an index of the red cell concentration. They (p. 31) give details of distribution of mepacrine in the tissues of experimental animals, and in various human secretions and tissues. Details should be sought in the original.

MARGRAITH *et al.* (p. 27) show that a prolonged trial of daily administration of mepacrine to 108 young women volunteers was followed in only one case by serious disorder and even that which was a psychosis, was not certainly due to the mepacrine.

FAIRLEY (p 398) shows that although in one area of New Guinea the failure of mepacrine suppression was largely due to faulty discipline, there was also a local, relatively mepacrine-resistant, strain of *P. falciparum* for which a double dosage was not too much. This strain was responsible for one-third of the overt attacks of *P. falciparum* malaria. Referring to this paper, STRAIN (p 398) states that discipline was no worse in the area concerned than in other areas, and that in that place it was never possible to arrange DDT spray, as was done elsewhere. He contends that there were many factors involved, and that variations in discipline may not have influenced the matter. FAIRLEY *et al* (p 399) investigated the mepacrine-resistant strains of *P. falciparum* referred to above, by inoculating them into volunteers. Even 0.2 gm mepacrine daily was not always effective in suppression, but paludrine in doses of 0.025 to 0.1 gm daily was a complete causal prophylactic. No evidence of mepacrine-resistant *P. vivax* was obtained. MACKERRAS (p 874) refers to this resistant strain of *P. falciparum* in Wewak, and remarks that similar resistance did not occur elsewhere, although for several months the troops were receiving inadequate amounts of mepacrine.

BANG *et al* (p 503) found malaria parasites in 14 per cent of a group of men under rigid mepacrine suppressive treatment, in which there had been only a few attacks of malaria, in a comparable group in which there had been much malaria previously, parasites were found in only 2 of 349. In Burma, under conditions of strenuous combat, 98 per cent of the men were protected by 1.0 gm mepacrine each week.

GOLDSMITH (p 502) reports successful suppression of malaria in labourers on an estate in Assam, who were given either one tablet of chloroquine once each week, or mepacrine each day. There were no cases of intolerance to chloroquine.

In *P. vivax* malaria (New Guinea infections) TRAGER *et al* (p 1036) found relapse rates of 61-76 per cent some 4-7 weeks after cessation of suppressive mepacrine in men whose acute attacks had been treated with mepacrine and other drugs. After treatment with quinine the relapse rate was 82 per cent.

BANG and HAIRSTON (p 1038) show that in a body of troops in the S. Pacific, the gametocyte rate in the men and the infection rate in mosquitoes varied in direct relation and argue that mepacrine suppression prevents infection.

ROBIN and BROCHEY (p 643) report a great reduction in parasite rates and spleen rates in African children (in Dakar) to whom mepacrine and rhodopraequine were given in several courses during a period of 4 months. PARRON *et al* (p 700) show that both mepacrine alone and mepacrine and pamaquin, given twice each week to the inhabitants of part of Algeria, were effective in prevention of attacks of malaria. The gametocidal action of pamaquin, however, was not considered enough to justify its inclusion.

FINDLAY (p 763) has reviewed a large amount of literature on the toxicity of mepacrine in man. Lichenoid dermatitis and other forms of dermatitis of mepacrine are critically discussed. The reader should consult the review itself for details. WILSON (p 395) discusses lichenoid dermatitis in relation to mepacrine. He thinks that this is the principal but not necessarily the only cause of the condition. KIERLAND (p 499) describes 49 cases of the eruption resembling lichen planus due to mepacrine. This almost invariably occurred in the older men at risk. The most serious complication was aplastic anaemia which was always fatal. CUSTER (p 697) reports that aplastic anaemia was much more common in men in the S. Pacific who were taking mepacrine than in those in areas where this was not necessary. In the 57 cases studied there was no evident correlation with any other drug and in 25 of them the anaemia was preceded by the atypical

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MARGRAITH and his colleagues (p. 496) found no indication that absorption of mepacrine was impaired by continuous administration of suppressive doses. In volunteers the mean plasma concentrations were about 26-28  $\mu\text{gm.}$  per litre on a dose of 0.1 gm. each day but individual variations were considerable. These workers (pp. 493, 499) working with volunteers, found that when 0.1 gm. mepacrine was given daily severe exercise under hot, moist conditions did not effect minimum mepacrine levels in blood or plasma, and that the final levels were not affected by the quantity of food taken, or by large amounts of cellulose. Elimination of mepacrine by the bowel varies between individuals, and may be quite considerable but it does not depend on failure of absorption.

SMITH *et al.* (p. 177) show that with small daily doses of mepacrine it takes 4-5 weeks to reach constant plasma levels with higher doses the time is shorter. BICKER *et al.* (p. 177) found plasma concentrations of atabrine [mepacrine] of 21.3 to 26 microgm. per litre in men taking 0.1 gm. each day. [The authors refer to levels of 21.3 G/L to 26.0 G/L, but explain that this represents microgrammes per litre. This use of the letter G is likely to lead to confusion.] In the *Archives of Internal Medicine* (p. 23) there is a report from the United States forces on plasma mepacrine levels. On 0.6 gm. each week the level rises slowly for 3-6 weeks, and then remains constant at about 30 microgm. per litre for each 1 gm. taken during one week. Priming doses of 0.3 gm. daily for 6 days raise the level more quickly. There is considerable individual variation in different people, and there is a group with very low levels this group was important in the war since it was necessary to give doses which would prevent malaria even in this group. A hot humid climate does not affect mepacrine absorption and storage there is no correlation between colouring of the skin and plasma mepacrine levels.

LEVINE and ERLANGER (p. 395) failed to find any effect of mepacrine administration on the electrocardiogram. BROWN and REMNIX (p. 497) discuss mepacrine metabolism in recurring *P. vivax* malaria.

BANG *et al.* (p. 281) found that mepacrine in a dose of 0.1 gm. each day was effective in suppression for troops in the S. Pacific a plasma level of 30 microgrammes per litre is satisfactory. In a series of cases of malaria in men who should have been taking 0.1 gm. mepacrine each day BROWN and REMNIX (p. 395) found that the usual reason for the apparent failure of suppression was that the men had, in fact not taken it regularly.

WILSON and ROBERTSON (p 1039) report on the use of DDT spray from aircraft in suppression of breeding of *A. gambiae* and *A. funestus* in East Africa. At a rate of 32 mgm per square metre breeding was immediately reduced by 98 per cent, the radius of control against these species need not be extended, in similar conditions, more than 1½ to 2 miles. The main application of this form of control (which is relatively costly) would be in inaccessible or very extensive areas, or where speed is necessary.

MACINNES (p 701) shows that larvicidal oils containing DDT have some lethal action on adult *A. gambiae* and *A. funestus* when the latter are kept in cages containing bowls of water covered with such oils.

For control of *A. melas* in the tidal marshes near Freetown, TREDRE (p 488) excluded tidal water from the belts of *Paspalum* grass and *Avicennia* mangrove, by embankments, drains and sluiceways with tidal flaps. He supplemented these measures by the use of larvicides, and by destruction of adults. For the control of *A. melas* in West Africa, THOMSON (p 795) thinks that bunding is probably the most effective method, but the siting and construction of the bund are affected by local conditions.

*A. sudaicus* breeds, south of Calcutta, in association with floating algae or submerged aquatic vegetation, but is inhibited by dense shade such as that given by the water hyacinth *Eschornia speciosa*. IYENGAR (p 564) has eradicated the larvae from ponds and swamps by cultivating this plant, and thinks that shade may act by killing the algae on which the larvae feed.

In the islands of Guadalcanal and Guam, during the war, dense forest was sprayed with DDT from aircraft as a means of mosquito control. HURLBUT *et al* (p 881) found that doses of 0.4 and 0.2 lb DDT per acre (in cyclohexanone and mineral oil) reduced adult mosquitoes and larvae by 98 and 99 per cent respectively.

Although conditions in 1945 favoured the breeding of *A. quadrimaculatus* in the Tennessee Valley, the expected outbreak of malaria did not occur, probably, as WATSON *et al* (p 801) suppose, because there were so few gametocyte carriers, owing to malaria control in the past. JONES *et al* (p 504) show that the 'para-para' isomer of DDT is about six times as toxic as the 'ortho-para' isomer, to larvae of *A. quadrimaculatus*. BRESCIA (p 881) has used DDT aerosols for killing larvae of *A. quadrimaculatus*, a dose of 0.001 lb DDT per acre killed almost 100 per cent within 12 hours.

DDT, in doses of 15-30 gallons of 5 per cent oil solution, emulsion or suspension, ensured about 75 per cent reduction of flies and mosquitoes, for 46 days, in salt marsh or jungle vegetation in the United States. Benzene hexachloride also gave promise of good results (MADDEN *et al*, p 1042).

In a comparison of DDT in the form of dust, spray and mist (in oil), and of paris green MATHIS *et al* (p 644) show that the DDT mist was the most generally useful in control of anopheline larvae. FERGUSON *et al* (p 645) give detailed information on the production of the DDT-oil mist.

In the Tennessee Valley Authority reservoirs many plants create problems associated with breeding of *A. quadrimaculatus*. HALL and HESS (p 1042) have experimented with 2,4-dichlorophenoxyacetic acid for control of growth of these plants, using it as a dust or as a spray. Details of the strengths of mixtures and solutions, and of method of application are given, this substance will probably prove more efficient and economical than mechanical means in the control of terrestrial plants and of most stiff-stemmed annuals, but it may have a deleterious effect on cotton crops in the vicinity, if it reaches them.

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lichen planus which has been associated with mepacrine. BAZEMORE *et al.* (p. 556) describe 314 cases of lichenoid dermatitis, and conclude that there is strong evidence that the condition is due to prolonged ingestion of mepacrine, but that the mechanism of action is not known. In susceptible persons mepacrine may produce acute erythema and oedema within a few days, with positive patch test or the lichenoid fixed eruption after 2-3 months ingestion. BUTLER (p. 792) discusses 247 patients in the S. Pacific, with atypical lichen planus; he is not convinced that mepacrine alone is the cause of the eruption, though it is most probably an aetiological agent. VIGANT (p. 877) also has reviewed the dermatitis due to mepacrine.

A blue-grey pigmentation of the nail-beds due to mepacrine is described by LUTTERLOH and SMALLENBERGER (p. 177).

AGRESS (p. 33) reports 5 cases of severe hepatitis and exfoliative dermatitis, of which 3 were fatal, due to mepacrine, and describes in detail the reasons for deciding that the drug actually caused these conditions in patients sensitive to it. A patch test with mepacrine will detect sensitivity. In an extremely sensitive person a toxic reaction may occur from ingestion of as little as 0.1 gm. of mepacrine.

### Control

MACDONALD (p. 182) has published a useful booklet on malaria and its control, written for planters and miners. This cannot be abstracted.

JAME (p. 178) shows that malaria increased in French North Africa during the war but that in 1944 there was an abrupt decline in incidence. Rainfall was deficient in that year and antimalarial measures of many kinds were renewed with materials from American sources which during the early part of the war had been lacking.

HOCKING (p. 1038) makes the point that as a measurement of the efficiency of control assessment of the number of cases of malaria is too slow and too unreliable. The results of hand-catching of mosquitoes are preferable, and a standard trap hut has been devised. Senior WHITE and RAO (p. 794) on the other hand, have confirmed the contention of Ribbands that the method of hand-catching fails to capture a very considerable proportion of mosquitoes in buildings; spraying with pyrethrum is much more effective for estimating the total mosquito population.

### Larvicidal Methods

SERGEANT and SERGEANT (p. 36) write of the value of colmatage which consists in causing silt-laden waters to deposit their silt in ponds and marshes, as an antilarval measure.

CAMBOURNAC *et al.* (p. 181) write very favourably of DDT in alcoholic solution as a larvicide for *A. maculipennis atroparvus* in ricefields: the alcohol ensures diffusion of the preparation. In ricefields in Kenya neither intermittent irrigation nor larvivorous fish reduced the number of anophelines but an oil-drop over the inlet channel was of value. GRAINGER (p. 844) shows, moreover, that intermittent irrigation probably decreased the crop.

WILSON (p. 156) shows very high incidence rates of malaria in European servicemen in various parts of East Africa during the war reduced as time went on and as control measures became more effective. The vectors were *A. gambiae* and *A. funestus* and the author thinks that though anopheline control may be very effective in controlling malaria for the greater part of the year larval control may fail to check the high seasonal incidence caused by *A. gambiae* in the more intensely malarious parts of East Africa. H. (p. 36) found powdered Derris root (2 lb. per acre) and Gammaxane (4 oz. per acre) effective larvicides, and gives the formula of a satisfactory oil which, at 5 gallons per acre, kills all larvae of *A. gambiae*.



WILSON and ROBERTSON (p 1039) report on the use of DDT spray from aircraft in suppression of breeding of *A. gambiae* and *A. funestus* in East Africa. At a rate of 32 mgm per square metre breeding was immediately reduced by 98 per cent, the radius of control against these species need not be extended, in similar conditions, more than 1½ to 2 miles. The main application of this form of control (which is relatively costly) would be in inaccessible or very extensive areas, or where speed is necessary.

MACINNES (p 701) shows that larvicidal oils containing DDT have some lethal action on adult *A. gambiae* and *A. funestus* when the latter are kept in cages containing bowls of water covered with such oils.

For control of *A. melas* in the tidal marshes near Freetown, TREDRE (p 488) excluded tidal water from the belts of *Paspalum* grass and *Avicennia* mangrove, by embankments, drains and sluiceways with tidal flaps. He supplemented these measures by the use of larvicides, and by destruction of adults. For the control of *A. melas* in West Africa, THOMSON (p 795) thinks that bunding is probably the most effective method, but the siting and construction of the bund are affected by local conditions.

*A. sundaticus* breeds, south of Calcutta, in association with floating algae or submerged aquatic vegetation, but is inhibited by dense shade such as that given by the water hyacinth *Eschornia speciosa*. IYENGAR (p 564) has eradicated the larvae from ponds and swamps by cultivating this plant, and thinks that shade may act by killing the algae on which the larvae feed.

In the islands of Guadalcanal and Guam, during the war, dense forest was sprayed with DDT from aircraft, as a means of mosquito control. HURLBUT *et al* (p 881) found that doses of 0.4 and 0.2 lb DDT per acre (in cyclohexanone and mineral oil) reduced adult mosquitoes and larvae by 98 and 99 per cent respectively.

Although conditions in 1945 favoured the breeding of *A. quadrimaculatus* in the Tennessee Valley, the expected outbreak of malaria did not occur, probably, as WATSON *et al* (p 801) suppose, because there were so few gametocyte carriers, owing to malaria control in the past. JONES *et al* (p 504) show that the *para-para*' isomer of DDT is about six times as toxic as the *ortho-para*' isomer, to larvae of *A. quadrimaculatus*. BRESCIA (p 881) has used DDT aerosols for killing larvae of *A. quadrimaculatus*, a dose of 0.001 lb DDT per acre killed almost 100 per cent within 12 hours.

DDT, in doses of 15-30 gallons of 5 per cent oil solution, emulsion or suspension, ensured about 75 per cent reduction of flies and mosquitoes, for 46 days, in salt marsh or jungle vegetation in the United States. Benzene hexachloride also gave promise of good results (MADDEN *et al*, p 1042).

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WESTPHAL and HORTON (p. 585) have successfully used tricalcium arsenite in place of paris green (but in twice the amount) in control of breeding of *A. pseudopunctipennis* in Peru.

#### Spray-killing of Adult Mosquitoes

UPHOLT (p. 645) discusses the inactivation of DDT in nature, especially its adsorption on mud. HARAWAY and BARLOW (p. 1036) find that only 6-15 per cent. of DDT (in oil) remains on the surface of mud bricks, the rest being adsorbed—a better result (82 per cent.) is obtained from treatment with a water suspension of dispersible powder.

GORDON (p. 801) did not observe ill effects in men engaged for several months in preparing solutions of DDT in kerosene, and applying them.

RIBBANS (p. 180) remarks that discovery of an efficient insecticide possessing no residual repellent or masking effect would be a considerable contribution to modern technique and shows that pyrethrum has a repellent action which lasts for at least 4 days. Lethane gives quicker knock-down than pyrethrum, and is less repellent but is more unpleasant. From careful experimental work, KENNEDY (p. 581) shows that DDT irritates mosquitoes, causing them to leave a treated surface more quickly than a non-treated surface, though not causing them to avoid the treated surface. In this sense it is a repellent and the dose the mosquitoes receive may be irritant but not fatal. The work was done with *Aedes aegypti* and *Anopheles maculipennis atroparvus*.

SWELLENGREBEL (p. 235) discusses malaria in Holland, pointing out that wartime destruction of a large number of domestic animals may force *A. maculipennis meuseus* to feed more on man, and therefore perhaps to become a more efficient vector. The most important vector is *A. m. atroparvus*. Spraying of houses with DDT may be a useful measure of control. Experience with pyrethrum spraying during 10 years was satisfactory even in the epidemic year of 1944 (SWELLENGREBEL and KRAAN, p. 236).

In a flooded area near the mouth of the Volturno River in Italy, ATTANI (p. 800) applied DDT in kerosene to all habitations, in January 1945. Thereafter it was found that the average anopheline density in human and animal houses was enormously reduced until autumn and was accompanied by great decrease in the numbers of larvae in the swamps. Spleen and parasite rates were reduced. Anophelines were relatively numerous near any untreated shelter and the author concludes that in such work all buildings should be sprayed. *A. maculipennis lebranchiae* and *A. sacharovi* were the predominant species. SOMER *et al.* (p. 877) refer to the work described by ATTANI and report similar work carried out in the delta of the Tiber where *A. m. lebranchiae* was breeding extensively in the flooded areas. DDT was sprayed in every house or shelter capable of harbouring anophelines, in spring 1945. The number of adults caught until late autumn was very low compared with previous records. Any unsprayed shelter greatly affected the numbers in the neighbourhood. The incidence of malaria declined continuously from March to the end of the year.

KARTMAN and DA SILVA (p. 38) show that relatively short contact with a DDT film in a glass tube is lethal to *A. gambiae* but in comment BURVING points out that all the DDT would be on the surface of the glass which is not the case with many other materials.

DR MENDONÇA and CRAQUEIRA (p. 983) show that *A. gambiae* continues to be found in aircraft arriving in Brazil from Africa. Inspection and fumigation of arriving aircraft are compulsory because of the danger of this and other pests.

WILSON (p. 179) notes that in partially closed buildings, for spray-killing mosquitoes, the direct hit is essential, and the average flat gun is not satisfactory. Against *A. gambiae* and *A. fuscatus* spraying is necessary every day in the evening. Pyrethrum is an essential constituent but some DDT should

be added THOMSON (p 795) has demonstrated the important fact that within a few days of treatment of houses, in Lagos, with DDT in kerosene, *A. gambiae* and *A. melas* enter the houses at night, feed, and leave without resting. There was no appreciable mortality within 48 hours in those that left in this way. Dramatic reduction in house catches after treatment with DDT is no proof that mosquitoes of these species are being killed. He discusses malaria in the Africans, and makes the point that it is not known to what extent malaria contributes to the ill-health of West African adults.

HOCKING (p 879) shows that residual spraying with DDT is effective against *A. gambiae* and *A. funestus* in that it does not interfere with normal entry into a building, but that the mortality in those that have been able to feed, and therefore tend to rest, is very high. He gives details of dosages, and information on the effect of the various surfaces to which DDT was applied. In relation to *A. gambiae* and *A. funestus* in the Gold Coast, EDDY (p 879) has found that spraying houses with DDT in kerosene, in various doses, is effective in reducing the numbers found at subsequent examination when counts were made of mosquitoes killed by pyrethrum spray [but see THOMSON above]. He calculates that such treatment would be needed every 2½ months, and notes that this method is more effective than continued spraying with pyrethrum, as was practised previously. In preliminary experiments on house-spraying with DDT against *A. funestus*, VINCKE (p 286) found that it does not prevent them from feeding, and has no repellent effect. Pyrethrum appears to have some initial repellent action, which gradually diminishes.

Senior WHITE *et al* (p 37) have published a critical review of the results attained in India by the spray-killing of adult mosquitoes with pyrethrum preparations, this has been more successful against *A. culicifacies* (which remains indoors, after feeding, until digestion is nearly complete) than against *A. minimus*. For the *A. fluviatilis* group, spraying for 6 days each week is the most effective, these mosquitoes leave the houses when digestion is only half complete, and are therefore vulnerable for spray-killing for only one daylight period in the cycle. Pyrethrum acts as a repellent to mosquitoes entering rooms. On the other hand, VISWANATHAN *et al* (p 38) think that for *A. fluviatilis*, spraying for 2 consecutive days followed by an interval of 1 or 2 free days, is satisfactory if antilarval methods are not possible.

In an experiment on control of rural malaria in India VISWANATHAN and PARIKH (p 798) conclude that residual DDT spray can be used economically and effectively, that a combination of spray-killing and larvicidal methods is too expensive, and that pyrethrum spray-killing is also too expensive.

Senior WHITE and GHOSH (p 799) have found DDT residual spray more effective against *A. fluviatilis* than against *A. culicifacies*, probably because the normal resting places of the former are walls and other places likely to have been sprayed, rather than furniture.

In relation to *A. minimus* in Assam, RIBBANDS (p 1041) found that spraying of houses with emulsions of DDT was more effective than with solutions, and that relatively heavy doses are preferable to light doses in view of their long persistence. Treatment of walls only, or ceilings only, may be effective. If the reduction of anophelines reaches 90 per cent there is, almost certainly, complete control of malaria transmission, but a repellent effect may be present which may reduce the actual degree of malaria control. Gammexane was also tested but on a smaller scale, its rôle is not yet established.

BRADLEY and FRITZ (p 180) show that residual spraying with DDT is very effective against *A. quadrimaculatus* greatly reducing the number found in houses for as long as 4 months, and also the number found to contain human blood.

FAY *et al* (p. 582) have tested the persistence of toxic effect of DDT when sprayed on certain surfaces under experimental conditions. *A. quadrimaculatus* was used in these tests. Residues from 100 mgm. per square foot were unreliable for lasting effectiveness. The same authors (p. 563) show how much the type of surface affects the residual toxicity. A dried mud surface is particularly bad, and grease and smoke deposits reduce the effectiveness of the DDT. TARRWELL and FISK (p. 583) show that in rooms sprayed with DDT the resting time of *A. quadrimaculatus* was very much shorter than in unsprayed rooms. They suggest that some unengorged mosquitoes may be sufficiently irritated by DDT to leave before feeding. As a result of tests of the effectiveness of DDT spraying of houses and barns as a measure of control of *A. quadrimaculatus* HESS and KREMER (p. 880) conclude that treatment of houses alone is inadequate, and that if all premises cannot be sprayed, it is better to treat barns in preference to houses, since this mosquito rests in barns during the daytime more frequently than in houses.

A comprehensive report from Panama on the effect of spraying houses with DDT on the density of *A. albimanus* and on the incidence of malaria, is given by TRAPIDO (p. 287). The anopheline density is dramatically reduced and remains relatively low for several weeks, and a considerable degree of control may be effected in this way but spraying 3 months before the period of great anopheline abundance is ineffective in preventing the normal increase. Figures are given which show the reduction effected in the incidence of malaria by this means. *A. albimanus* is a wild mosquito which seldom remains long in houses. Nevertheless STEPHENS and PRATT (p. 564) found that spraying of houses in Porto Rico with DDT twice in one year produced a significant reduction in the parasite rate of the inhabitants.

GIGLIOLI (pp. 181-504) has found that *A. darlingi* is particularly vulnerable by DDT. Females rest on the walls of houses before and after feeding. In sprayed houses in British Guiana great reduction in specimens captured in dwellings was observed during 9-10 months after spraying, and there was a significant fall in spleen and parasite rates in the people.

GAHAN and PAYNE (p. 880) show that spraying of villages with DDT not only very greatly reduced the number of adult *A. pseudopunctipennis* for several months, but reduced also the number of larvae found breeding in the adjacent ricefields.

### Malaria of Monkeys Birds etc.

GARRHAM (p. 882) describes his discovery of exoerythrocytic forms of *P. falciparum* in *Cercopithecus* monkeys in Kenya. These bodies were found in the livers of 15 of the monkeys, and the author gives his reasons for considering them to be exoerythrocytic forms of this parasite. [This is the first occasion on which such forms have been described in mammalian plasmodia.]

In the Report of the Scientific Advisory Board of the Indian Research Fund Association for 1946 (p. 966) there is an account of the attempt made in India to find exoerythrocytic forms of *P. cynomolgi* in monkeys. The attempt was not successful, but a lot of information was obtained on mosquito transmission, transmission by injection of sporozoites, and infectivity of blood and various organs at different stages after infection.

WOLFSON and WINTER (p. 585) describe the course of *P. cynomolgi* infection in rhesus monkeys. TALLAFERRO and TALLAFERRO (p. 935) describe the course of asexual reproduction in *P. cynomolgi*.

MAJUMDER and DAS GUPTA (p. 183) describe the blood picture of normal *Macaca rhesus*, and discuss the anaemia produced in them by *P. knowlesi*. MCKEE and his colleagues (p. 1043) have studied the chemistry and metabolism of monkey blood, both normal and infected with *P. knowlesi* and

describe apparatus in which cultures can be maintained *in vitro*. Subcultures have been made for 7 generations, the parasites remaining infective. These papers contain much detail, and the originals should be studied.

SHEN *et al* (p 1045) find that red cells containing *P. knowlesi* develop increased osmotic fragility and are destroyed by mechanical trauma more easily than normal cells. This may be the basis of the haemolytic anaemia of malaria.

McKEE and GEIMAN (p 649) report work which indicates that the plasma level of ascorbic acid in monkeys infected with *P. knowlesi* is lower than the normal, and also that in monkeys rendered deficient in this vitamin, induced infection is less acute than in normal controls, such monkeys appear able to acquire immunity and control the infections.

RICHARDSON *et al* (p 289) have investigated the course of *P. knowlesi* infection of monkeys after measured infections, and have assessed quantitatively the great superiority of sulphadiazine over quinine in treatment.

EKZEMPLARSKAYA (p 182) shows that monkeys infected with *P. imui* become immune to the same strain, but not to other strains of the same parasite. He also shows that the humoral factor in the defence mechanism is insignificant in comparison with the cellular factor.

PEEL and RODHAIN (p 967) describe the schizogony of *P. reichenowi* in a chimpanzee. RODHAIN and LASSMAN (p 184) discuss the cultivation of the malaria parasites of chimpanzees, by the method of Bass. RODHAIN (p 801) describes a new malaria parasite of the gibbon.

WOLFSON and CAKRTOVA (p 566) discuss the relationship between the number of parasites and infected red cells in bird and monkey malaria.

STAUBER and WALKER (pp 967, 1046) describe a method of preparing suspensions of avian malaria parasites almost entirely free of any trace of red cell substance.

SEELER and OTT (p 185) discuss the effect of deficiencies in vitamins and protein on avian malaria.

DEARBORN and MARSHALL (p 568) find that various species of avian malaria parasites differ in their response to different drugs, and that a single species, therefore, is not satisfactory for the purpose of selecting drugs for test. MARSHALL and DEARBORN (p 292) show that in avian malaria a single daily dose of a drug may give results worse than, equal to, or better than those obtained by continuous drug-diet administration, according to the drug used.

TREMBLEY (p 402) has shown that *Aedes atropalpus* is a potential vector of *P. gallinaceum*. HOVANITZ (p 566) shows that there is little variation in infectibility of individual *Aedes aegypti* with *P. gallinaceum*. CANTRELL and JORDAN (p 39) show that the maximum number of oocysts occurs in *Aedes aegypti* when these mosquitoes feed on chickens infected with *P. gallinaceum* the day before the peak of parasitaemia, they discuss the possible reasons for this.

GORDON and HILL (p 402) describe their technique for obtaining suspensions of infective sporozoites of *P. gallinaceum*, which are bacteriologically sterile, from the salivary glands of mosquitoes.

TERZIAN (p 969) shows that splenectomy during the latent period adversely affects chicks infected with *P. gallinaceum*, though not those with the milder *P. lophurae* infection. This indicates that the lymphoid-macrophage system is actively involved in these infections.

CEITHAML and EVANS (p 567) exposed red cells containing *P. gallinaceum* to X-ray, and then injected them into clean fowls. High doses of X-ray reduce the infectivity of the parasitized cells, partially or entirely, but injection of these cells confers some immunity, as tested by subsequent injection of infective blood.

TALLAFERRO and TALLAFERRO (p. 40) report that chickens infected with *P. gallinaceum* show strong immunity to the same species and to *P. lophurae* but that chickens infected with *P. lophurae* show only slight immunity to *P. gallinaceum*.

Downs (p. 1045) shows that single trophozoites (*P. gallinaceum*) injected into normal chicks, give rise to schizogamous gametogamous and exoerythrocytic cycles.

TOLLIS (p. 968) describes the distribution of exoerythrocytic forms of *P. gallinaceum* in chicks, after blood infection. HAAS *et al.* (p. 290) describe their methods in obtaining heavy exoerythrocytic infections of chicks with *P. gallinaceum*; for details the original should be consulted.

BRACKETT *et al.* (p. 291) have shown that infections with *P. gallinaceum* in chickens taking a diet deficient in pantothenic acid are much less severe than in controls, and that pantothenic acid is necessary for the erythrocytic stages of this parasite. The exoerythrocytic forms probably find enough pantothenic acid in their particular habitat. Analogues of this substance have an anti-malarial action in blood-induced, but not in sporozoite-induced, infections, and this is antagonized by pantothenate.

ZUCKERMAN (p. 504) has studied infections of chick embryos with *P. gallinaceum* induced by implantation of emulsions of brain containing exoerythrocytic and erythrocytic stages on to the chorio-allantoic membrane, and by intramuscular injection of blood containing erythrocytic forms. It seems that infection through the membrane is effected only by the exoerythrocytic forms. Parasites in embryonic spleen can be grown by a tissue-culture method, and by exposing such spleens, containing exoerythrocytic forms, to various drugs, and then making tissue cultures, the effects of the drugs can be estimated.

MEYER (p. 968) has cultivated the erythrocytic form of *P. gallinaceum* in tissue cultures of embryonic chicken brain.

TONKIN (p. 184) tested a number of drugs against exoerythrocytic forms of *P. gallinaceum* in tissue culture; for details the original should be consulted.

BRACKETT *et al.* (p. 40) describe the antimalarial effects of metachlorodine against *P. gallinaceum* and in human malaria. It can act as a causal prophylactic against *P. gallinaceum* and is effective against *P. cathemerium* (HUGHES and BRACKETT p. 41).

CARLSON *et al.* (p. 39) have found that extracts of various plants are not only effective bactericidal agents, but also are lethal to *P. gallinaceum*: *in vitro*.

GINGRICH *et al.* (p. 803) obtained radical cure of *P. cathemerium* infections with a naphthoquinone derivative.

BALL (p. 1045) has attempted to cultivate the mid-gut of *Culex tarsalis* containing oocysts of *P. relictum*, but although the stomach remained alive for 10 days, the oocysts did not develop.

COULSTON and HUFF (p. 970) describe the morphology of pre-erythrocytic forms of *P. relictum*. HAWKING (p. 970) has grown exoerythrocytic forms of *P. relictum* in tissue culture.

TRAGER (p. 1046) used a complicated medium for the cultivation of *P. lophurae*. True multiplication of the parasite occurs, and physiological studies are therefore possible.

HUFF *et al.* (p. 1046) have studied pre-erythrocytic forms of *P. lophurae* in turkeys, ducks, chickens and guinea fowl. They conclude that it is no longer possible to measure susceptibility of the host solely by the degree of parasitaemia, since some parasites exhibit numerous pre-erythrocytic forms, but only a mild blood infection. They give four criteria by which the suitability of a host for a given parasite may be measured.

RIGDON and VARNADOE (p 505) show that *melanophils* from the spleen in an oxygen chamber than in air, and they discuss the *contribution* of *melanophils* in human malaria. ROSTORFER and MCGEE (p 567) *in a study* of *oxygen* saturation of ducks infected with *P. lophurae* *in the* *oxygen* saturation of ducks infected with *P. lophurae* is *not* *fully* *satisfactorily* be condensed further. RIGDON and ROSTORFER (p 568) *have* shown that death of birds infected with *P. lophurae* is *caused* by *failure* of the blood to carry sufficient oxygen to support life, at the time of death it may have only 20 per cent of the normal oxygen capacity. FLETCHER and RIGDON (p 42) observed neurological disturbances (ataxia etc.) in *ducks* which had recovered from *P. lophurae* infections, and think that *these* *may* have been due to anoxia, the result of anaemia, aggravated by *vascular* *instability*. RIGDON (p 884) shows that deficiency of vitamin A *does not* significantly affect this disease, and RIGDON and MARVIN (p 884) that insulin injections do not affect it. SEELER and OTT (p 41) show that *P. lophurae* infection in chickens on low-protein diet runs a much more severe course than in those on high-protein diet, even if total serum protein is normal. It is known that hypoproteinaemia interferes with antibody production.

Roos *et al* (p 403) have investigated the different effects of deficiency of various vitamins on *P. lophurae* infection of chickens and ducks.

MARSHALL and DEARBORN (p 292) have shown that in ducks infected with *P. lophurae*, and treated with mepacrine, similar plasma concentrations produced in individual birds by different doses are not equally active against the infection. Great variations were found in different birds given the same dose, and these are probably due to differences in distribution between plasma and tissues (including erythrocytes).

WOLFSON (p 568) shows that *P. elongatum* attacks immature erythrocytes of ducks, and is a very fatal infection in spite of relatively low rates of parasitaemia. *P. lophurae*, on the other hand, attacks mature red cells, produces severe parasitaemia, but not so severe anaemia.

MANWELL (p 43) describes certain malaria parasites of bats.

THOMPSON (p 43) shows that the action of quinine on the malaria parasites of lizards is similar to its action on the plasmodia of various warm-blooded animals. THOMPSON (p 569) has observed the effects of mepacrine on the lizard malaria parasite, *P. floridense*.

Charles Wilcocks

## RABIES

LEPINE, P. & ATHANASIU, P. Contamination spontanée du lapin par le virus de la maladie de Borna. Spontaneous Infection of a Rabbit with Borna Disease, *Ann Inst Pasteur* 1947, Aug, v 73 No 8, 827-8.

This note records the fate of one of a batch of 8 rabbits which had been used to titrate rabies virus by inoculation of brain substance from a rabbit *probably* infected with rabies. The titres employed were not lethal to 7 of the rabbits, the eighth died but histological examination demonstrated beyond doubt that the animal extended the lesions not of rabies but of Borna disease. The latter disease could be reproduced experimentally in fresh rabbits. The source and mode of the infection is discussed and it seems to be likely that it was derived from another rabbit known to have Borna disease, which had





LÉPINE, P & ATHANASIU, P Evolution des lesions histologiques et des anticorps rabiques aux cours de l'incubation de la rage des rues [Development of Histological Lesions and of Rabieidal Antibodies during the Incubation Period of Street Virus Rabies] *Ann Inst Pasteur* 1947, Aug, v 73, No 8, 824-7

The time when the first histological lesions appear during the incubation period of rabies is of much theoretical and practical importance. Could it be demonstrated that the first lesions in the brain occur before the saliva becomes virulent, it would be possible to exempt from treatment persons bitten by an animal showing no symptoms of rabies and dead before the expiration of its period of observation. Of theoretical interest would be the establishment of a relationship, should such exist, between the occurrence of cellular lesions and that of serum antibodies.

To settle these questions, the authors inoculated 14 rabbits by the intracerebral route with a street virus strain (Corsican strain I), of which the full development in the rabbit regularly exceeds 18 days and averages 20. From the 48th hour after inoculation, the authors killed one rabbit every second day then from the 16th to the 20th day one rabbit every day. The brain, the two Gasserian ganglia and 1.5 cm of the main trunk of the sciatic nerve were removed from each animal for histological examination, and parts were inoculated into mice for proof of the presence of virus. Moreover, before being killed the animal was bled and its serum titrated with suspensions of the same street virus strain to determine the existence of neutralizing antibodies.

From these experiments it emerged that, after the intracerebral inoculation of rabbits with the particular street virus strain employed, the first lesions in the brain appeared about the 4th day, while the brain became virulent only on the 8th day and death did not supervene until the 18th day at the earliest. The Gasserian ganglia showed lesions on the 8th day and gave evidence of virulence on the 10th. In the sciatic nerve, lesions were demonstrable on the 10th day, virulence was present on the 12th but, whereas virus remained in the brain up to the moment of death, there was observed in the Gasserian ganglia and in the sciatic nerve a diminution, indeed a total disappearance, of virulence from the 18th day.

Antibodies, which first made their appearance in the serum on the 10th day thereafter showed a regular increase up to the time of the animal's death, when a very high content was achieved.

G. Stuart

JACOTOR, H Le gel d'alumine comme adjuvant du vaccin antirabique formolé [Alumina Gel as Adjuvant to Formolized Antirabic Vaccine] *Ann Inst Pasteur* 1947, Oct, v 73, No 10, 1028-30

The author had previously placed on record the 10-to-25-fold increase in immunizing power conferred by the addition of aluminium hydroxide to anti-cattle-plague vaccines made from formolized organic pulp. A similar procedure permits a reinforcement of the formolized antirabic vaccine in current use in many countries for prophylaxis against canine rabies.

The technique of preparation is briefly as follows: dogs are inoculated with fixed virus rabies by the intracranial route when they are completely paralysed, they are killed and their brains extracted. The infected brains after being finely ground in a mortar are emulsified with a little formolized water, after filtration through gauze the emulsion is placed in an incubator for 24 hours at 37°C, thereafter it is kept for 4 days at the temperature of the environment (25°-30°C). The emulsion is then divided equally, to one part is added an amount of alumina gel equal to or somewhat less than the mass of nervous

matter finally sufficient water is added to ensure a resulting dilution of 1 : 8. The remaining half is brought to the same volume with plain water and serves as the control vaccine.

Five sets of adequately controlled experiments were made, during which guineapigs in parallel series had been inoculated with a twice-repeated dosage, at three weeks intervals, of from 0.25 cc. to 2.0 cc. of either gel or non-gel vaccine—this had been kept at room temperature before use for periods ranging from 15 days to 7 months, at the end of which time a test dose of 0.02 gm. of street virus was administered in the masseters 3 to 5 weeks after completion of treatment.

It was found that vaccine, with gel added, protected 81 per cent. of the relevant guineapig series, while the control vaccine protected only 44 per cent. and that the test dose, which killed all the unvaccinated control animals, killed 3 times as many guineapigs protected by the ordinary formalized vaccine as those treated with gel-added vaccine. The author therefore concludes that the alumina gel clearly reinforces the protective power of antirabic vaccines prepared from formalized emulsions of brain pulp.

Finally it should be noted that in the case of the vaccine concerned, the action of the alumina gel is on a tissue pulp rendered wholly avirulent by the addition of formal.

G. Stuart

GHODSI M. Dix années de traitement antirabique à l'Institut Pasteur de l'Iran (Téhéran) 1936-1945. [Ten Years of Anti-Rabies Treatment at the Pasteur Institute of Iran (Tehran) 1936-1945.] *Ann. Inst. Pasteur* 1947 Sept. v 73 No 9 900-902.

The author intimates that there was a change during 1936 in the method of anti-rabies treatment practised at Teheran from vaccination with dried cords to the use of 5 per cent. fixed virus rabbit brain in 1 per cent. phenolized water killed by exposure to 37°C. in the incubator for 24 hours.

The usual course of treatment is the daily administration subcutaneously in the abdomen of 6 cc. on 20 successive days, but in the case of severe wounding (multiple bites on the face) the daily injections are extended to 30 days.

No decentralization of treatment is possible.

During the 10 years of treatment with phenolized vaccine, there have been 38 deaths—most of these occurred at the beginning, middle or end of treatment some few one or two days after its completion. Of these deaths, 36 followed wolf bites, 1 was from dog bite and 1 from jackal bite. In all 38 cases there was considerable delay in reporting for treatment—a delay averaging 15 days from the time of biting (minimum 5 days, maximum 32 days).

During the 10 years under review no case of neuroparalytic accident was observed among the 2,135 bitten persons treated.

G. Stuart

REMLINGER, P & BAILLY J. La rage du loup: critérium de l'efficacité de la vaccination pasteurienne. [Rabies in the Wolf: Criterion of Efficacy in Pasteurian Treatment.] *Bull. Acad. Nat. Méd.* 1947 v 131 No. 30/31 597-9

The authors recall recent criticism regarding the efficacy of anti-rabies treatment by Pasteur's method. In their view definite proof of efficacy would be furnished by a statistical study of the results of treatment in cases of wolf bite. They point out that wolves are almost certainly rabid if they bite human beings and that the incubation period of rabies after bites by these animals is shorter than that for other animals. In the past there have been many instances of death in those actually under treatment.

The suggestion is made that in cases of severe wolf-bite the intensive method of treatment advocated by FERRAN should be adopted. The basis of this treatment rests on the assumption that the addition of bichloride of mercury to an emulsion of fixed virus gives a chemotactic effect to the inoculated material which results in the retention in the peripheral circulation of leucocytes, which otherwise might transport a quantity of virus by the blood stream to the central nervous system.

The authors further suggest increased doses at diminished intervals, compared with the dosage and interspacing followed in the classical treatment, they add that with killed virus vaccine the paralytic accidents previously encountered with massive dosage need not now be feared.

G. Stuart

PUBLIC HEALTH REP. Wash. 1947, Aug 22, v. 62, No 34, 1215-37 [30 refs.] **Control of Rabies** Report by the Committee on Public Health Relations of the New York Academy of Medicine

The control of rabies in the United States has been studied and reported on by the Committee on Public Health Relations of the New York Academy of Medicine. Although the report under review is but an abridgement of the full Report, nevertheless the shorter version contains so much of value to those interested in rabies control that no abstract could hope to do justice to the many aspects of the problem treated. The reader is advised, therefore, to obtain and study the original document.

In the following review only the more important points receive consideration —

Between 1938 and 1945, the average annual incidence of reported rabies in animals in the U.S.A. was 8 775, with the last three years of the series above average. 1945 was the peak year. Notifications, however, are regarded as incomplete. Rabies occurred mainly among dogs, but many other animal species were affected. An epizootic among foxes has troubled the south-eastern States for some years.

One of the major difficulties in securing effective control over the disease is the lack of uniformity between States and counties within States of notification procedures and control measures. Thus in some States rabies in animals is not even notifiable and the laws regarding the licensing and vaccination of dogs follow no common pattern. A similar diversity exists in the laws regarding quarantine and the inter State movement of animals. This lack of legislative uniformity is reflected in the innumerable agencies charged with the enforcement of such control laws as exist. SCOTTING in the Yearbook of Agriculture for 1942 aptly sums up the existing situation. Rabies is an outstanding example of a dangerous disease which could be controlled or eventually

5 cc. of potent vaccine is recommended for dogs, when rabies has been reported in the area. Three injections administered at weekly intervals, are, however, regarded as producing a more certain immunity. This latter method was practised yearly by the U.S. Army during the Second World War and only one case of rabies developed among 19 050 dogs so immunized. In the case referred to it is possible that the routine vaccination had not been carried out.

The common line of control measures in the presence of established cases in various States has been—mass vaccination of dogs, free of charge to the owners; enforcement of quarantine laws; collection and disposal of stray dogs; and appropriate education of the general public.

The Report also includes a review of recent scientific developments, including the mouse inoculation test devised by WHESTER & DAWSON in 1935 [this *Bulletin* 1935 v 32, 603]. This method is stated to give 10 per cent. of positive results in cases where Negri bodies had not previously been demonstrated. Stress is also laid upon the superior potency of vaccine irradiated with a new type of extreme ultra-violet lamp described by LARIVINSON *et al* in 1944 [*ibid* 1944 v 41 914], as compared with phenol or chloroform-treated vaccines or with vaccine irradiated by ordinary ultra-violet light. Protection by this special irradiated vaccine has been given against 20 000 M.L.D. compared with 2,477 M.L.D. for a control phenolized vaccine. Potency is said to be good after storage; no appreciable loss being detected after six months.

Reference is again made to the suggestion of HANAL [*ibid.*, 1946, v 43 187] that the use of immune serum alone or in combination with vaccine given after a period of 8 days may effectively protect man against rabies.

Finally a series of recommendations by the Committee is submitted, urging the adoption of National control measures. The Federal agencies concerned, in co-operation with appropriate State agencies, should draw up a plan for the eradication of rabies. The inter State transportation of susceptible animals should be regulated and provision made for the control of animals entering the United States from foreign countries. Rabies should be made universally reportable. The annual licensing and vaccination of dogs is recommended with the suggestion that in urban areas the granting of licences should be contingent on vaccination. Three injections of 5 cc. of a potent vaccine at weekly intervals are recommended as constituting the method of choice, but a single shot injection of 5 cc. is of benefit when mass vaccination programmes are being carried out and triple inoculation is not practicable. Recommendations to promote control also include the quarantine and impounding of dogs during outbreaks. Educational campaigns should also be launched, giving publicity to the measures adopted.

G. Stuart

IOJESCU D. Importanța vaccinării antirabice preventive și obligatorie în masa a câinilor în profilaxia turbarii. [The Importance of Mass Vaccination of Dogs in the Prevention of Rabies.] *Rev. Științ. Med.* Bucharest. 1946 May-Aug v 35 No. 5/8 424-30. French summary.

A wild strain of rabies virus obtained from a wolf was adapted to dogs by serial passage. At the present time the strain has undergone more than 300 passages, and the incubation period has become stabilized at 7 days. A phenolized vaccine has been prepared from the strain, and is considered to be more effective in immunizing dogs than one utilizing a strain of virus adapted to some other mammalian species. The use of the vaccine is devoid of risk, and it is suitable for the mass vaccination of dogs which is considered to be a rational and practical method for reducing the incidence of rabies. Experience of mass inoculation in other countries is briefly reviewed.

D. J. Baxter

NOVICKY, R. Aportación al estudio de la rabia parolítica bovina en Venezuela [Bovine Paralytic Rabies in Venezuela.] *Bol Inst Invest Vet Caracas* 1946, Dec 3 No 13, 399-468 [35 refs.] English summary

## MALARIA

DE MEILLON, B. The Anophelini of the Ethiopian Geographical Region. *Publications of South African Inst Med Res* 1947, Sept, v 10, No 49, 272 pp, 85 pls 1 map & 2 figs Johannesburg The Librarian South African Institute for Medical Research, Hospital Street [30s]

Students of African anophelines will welcome the appearance of this work as it brings together available knowledge and an up-to-date classification of these mosquitoes. The book is intended for those who already have some knowledge of the subject therefore there is no general account of mosquito morphology. Nearly a hundred species and varieties of *Anopheles* are dealt with, they occur in the continent of Africa south of the Sahara, the islands around it and a small portion of Arabia. Classification is based largely on the works of Root, Christophers, Edwards and Evans, with some modifications. Adult characters are used principally for the identification of subgenera and groups and larval characters for the identification of series. Subgroups have been abandoned in favour of series in order to maintain uniformity.

Phylogeny, zoogeography and the relationship of the species to malaria are briefly discussed, and breeding places are broadly classified. Keys are provided for the separation of subgenera, groups and series, there are also keys to females and to fourth stage larvae. The keys to pupae and to eggs are for the moment tentative as they will need revision as more precise information is accumulated.

The main bulk of the book (some 200 pages) is taken up with systematic descriptions of the species, though these are limited to the bare essentials. The chief distinguishing morphological features of most of the species are illustrated by numerous line drawings. Descriptions of pupae are not included in this section, as there is considerable doubt about the accuracy of some of the published descriptions. For each species there are notes on breeding places, relation to malaria and on distribution. At the end of the book there is a summary of the known geographical distribution of the species in tabular form, a valuable bibliography occupying eight pages and a most clearly arranged index.

The true value of a book of this nature can only be assessed after a period of use and reference, but there is no doubt that this publication is most timely. Both the morphological and the biological details have been most carefully assembled, and from the frequent notes which follow many of the descriptions, one gains the impression that the author has been to considerable pains to include ideas and results from the latest investigations. The general matter is of necessity somewhat condensed but in view of the extensive bibliography provided, not unreasonably so. For example, the important species *Anopheles gambiae* and *A. funestus* receive fourteen and eight pages respectively, but in each case only two pages are taken up with morphology, the remainder being devoted to biological matters. Other species of less medical importance are quite adequately dealt with in a page or two. Some species are of course not yet so thoroughly known, but as knowledge increases it becomes evident that previously accepted ideas about species relationships and species distribution must be modified. To take one point, cited by the author, *A. brunnipes*, a

species formerly known only from Angola and the Belgian Congo and recently shown to be a vector of malaria, is now recorded from Portuguese East Africa and the Rhodesias.

Modern methods of study including the rearing of species through all stages from the egg to the adult, comparison of certain morphological characters such as the female pharyngeal armature, male terminalia and pupal paddles, have provided the worker with further clues to these relationships and have all combined to assist in the accurate identification of these important insects. For some time to come this book will be regarded as a major reference work on the subject of African anophelines.

H S Lesson

SCHWITZ, J. Recherches sur les moustiques dans la bordure orientale du Congo Belge (Lac Kivu-Lac Albert). [Studies of Mosquitoes in the Eastern Border of the Belgian Congo.] Institut Royal Colonial Belge. Section des Sciences Naturelles et Médicales. Mémoires. (Collection In-8°) 1944 v 14 No. 1 93 pp. 8 maps (1 folding) & 9 figs. on 2 pls. [11 refs.]

The author collected 88 species of mosquitoes (15 Anophelines, 1 Megarthine and 52 Culicines) during a journey along the eastern border of the Belgian Congo between July and November 1939—this period covered part of the dry season and part of the wet season, and the country investigated ranged from south of Lake Kivu to the north of Lake Albert.

This publication contains annotated records of the collection arranged by localities, which are briefly described. There are sketch maps of some of the areas, as well as a map of the whole region showing the route followed. The substance of the paper is mainly entomological and is not easily summarized; those interested would in any case have to consult it in the original. The collections are deposited partly in the Museum of the Belgian Congo at Tervueren, Belgium, partly in the British Museum (Natural History) and partly in the Laboratory of Parasitology of the University of Brussels.

H S Lesson

KALANDADZE L. P. & KAVILADZE O. P. (On the Blood-Sucking Mosquitoes of the Western Part of the Iran Azerbaijan.) Med. Parazit & Parasitic Dis. Moscow 1947 v 16 No. 1 57-65 3 figs. [In Russian.]

With the view to filling the gap in our knowledge of the mosquito fauna of the Azerbaijan province of Iran the authors have made collections and observations in the course of two years, the results of which are described in this paper. Mosquitoes in this area are represented by the following forms: (1) *Anopheles maculipennis* is ubiquitous, of the two subspecies present *A. m. maculipennis* is widely distributed, while *A. seckeri* has a restricted distribution. This species is the most dangerous local vector of malaria. (2) *A. claviger* (*bifurcatus*) was found in Khoi and Maraga. (3) *A. algeriensis* which is a rare species, occurs in Maku. (4) *A. plumbeus* was seen once in Khoi. (5) *A. (Mynomyia) superpictus* is widespread, being second only to *A. maculipennis*. (6) *Theobaldia (Allothobaldia) longiareolata* is comparatively rare—it was encountered in Khoi, Maku and Sharif Khana. (7) *T. alaskensis* is rare, probably restricted to mountainous regions—found in Maku. (8) *T. annulata* is the most common species of this genus, occurring in Khoi, Maku, Shahpur Ruzeh. (9) *T. annulata subochrea* was found only in Khoi. (10) *Aedes (Ochlerotatus) caspius caspius* occurs in Khoi, Shahpur Maku, Beshkez and Tabriz. (11) *A. (O.) c. dornalis* is first recorded for Iran—it occurs in Khoi, Shahpur Maku, Tabriz and Sharif Khana. (12) *A. (Aedimorphus) vexans* is found in Beshkez and Khoi. (13) *Culex (N. culex) deserticola*. One specimen only seen in Maku, but its identity

needs confirmation (14) *C (N) hortensis* a very rare species encountered in Karavan-Sarai and Maku (15) *C theileri* is fairly widespread, found in Khoi, Maraga, Maku and Karavan-Sarai (16) *C pipiens*, though known to be common, relatively few specimens were collected in Maku, Rizaeh, Ushna, and Maraga. Among the malaria vectors the most common and dangerous species are *Anopheles maculipennis maculipennis* and *A. superpictus*, while the most common culicines are *Aedes caspius*, *Culex theileri* and *C. pipiens*.

The authors further give some phenological data on the anophelines of Iranian Azerbaijan, viz, time of flight after hibernation, time of appearance of first aquatic stages, flight of first males and number of generations, preparation for hibernation. It is noted that all water collections play an important rôle in the distribution of the malaria vectors, but especially those which are connected with the irrigation system. Anopheline mosquitoes were encountered in dwellings of different types, including dug-outs and tents, as well as in barns and cellars, but they were especially numerous in animal-houses. Though the buildings do not provide the mosquitoes with shelter during the malarious season, they congregate there in large numbers for hibernation.

C A Hoare

BEKLEMISCHEV, W N & SHIPITSINA, N K [*Anopheles marteri* in the North-Western Iran] *Med Parasit & Parasitic Dis* Moscow 1947, v 16, No 1, 66-7, 3 figs [In Russian].

The authors record the first finding of *Anopheles marteri* in the valley of the river Yuzbashchai of north-western Iran. It is noted that although the distribution of this species covers all the Mediterranean region from Spain and Algeria to Thrace and Syria, and extends to the mountains of Middle Asia, it has hitherto not been discovered between Syria and Tadjikistan. The present finding helps to fill the gap and leads one to expect to find this species in Southern Transcaucasia, including the mountains of Southern Azerbaijan [Iran] and Armenia. A description is given of the characters of the larvae of this mosquito.

C A Hoare

WOODHILL, A R. Observations on the Morphology and Biology of the Subspecies of *Anopheles punctulatus* Dönitz. *Proc Linnæan Soc New South Wales* 1945, v 70, Pts 5/6, Nos 321/322, 276-87, 1 map and 3 figs.

This paper is a further contribution to the discussion on the relationship and status of the forms of the Australasian anopheline mosquito occurring within the species *Anopheles punctulatus*.

The author holds that there are two subspecies (not species) *A. p. punctulatus* and *A. p. farauti* which may be differentiated morphologically by the palps in the adult and by the shoulder hairs in the larva. Certain other differences in larvae are not constant over the whole range of the species, but only in certain areas.

Besides these two subspecies, intermediate forms exist which the author believes to be hybrids, and this idea is supported by evidence produced from field observations, for where one subspecies is present alone no intermediates have been recorded, whereas breeding experiments show that both adult and larval progeny of intermediate females exhibit all variations from the *A. p. punctulatus* to the *A. p. farauti* type.

It is essential that workers should attempt to cross one subspecies with the other on a large scale and demonstrate finally whether inter-fertility occurs.

With reference to *A. kolensis*, which appears to be constant in its characters in the Solomon Islands, specimens from New Guinea cannot be considered as

such, because they give rise to both *punctulatus* and *farauti* in their progeny, the author is therefore of the opinion that it is more logical to regard *kohuensis* as a subspecies of *punctulatus* than as a distinct species. H S Lesson

HARDMAN V F Studies on Imported Malaria. 3. Laboratory Rearing of Western *Anopheles*. J National Malaria Soc. 1947 Sept. v 8, No. 3 165-72.

This paper concerns the insectary rearing of *Anopheles maculipennis fressborni* in California and includes some notes on *A. m. occidentalis*, *A. punctipennis* and *A. pseudopunctipennis franciscanus*.

The insectary was a dull-white painted room of 1 050 cubic feet, provided with natural as well as fluorescent lighting. The temperature was about 28°C. and the relative humidity was between 80 and 85 per cent. Larvae were kept in shallow rectangular pans in water from the breeding place and only one batch of larvae was reared in the same water. The larval food was a mixture of 90 per cent. finely ground dog-food with 10 per cent. yeast. This mixture was dusted on to the water surface daily from the second or third day after the hatching of the eggs. Pupae were recovered daily and transferred to cartons, into which two or three large larvae were placed to consume the surface scum; this procedure reduced the previously very high mortality among emerging adults to about 4 per cent. All pipettes were rinsed in alcohol between moves, to prevent the contamination by bacterial scum being transmitted from one pan to another.

In seven months, 89,500 pupae were obtained and seven generations were passed through. The period from oviposition to pupation averaged 21 days over a range of 12 to 30 days at a water temperature of 27°C. Adults reared from larvae kept at 100 to 200 per square foot of water surface were smaller than field-collected adults, but those reared from larvae kept at 10 per square foot were about the same size.

Attempts to rear *A. m. occidentalis* and *A. punctipennis* have so far failed. A few attempts to obtain mating of *A. pseudopunctipennis franciscanus* were successful, but only in cages 14x14x36 inches or larger. It was found necessary to give blood-meals to females of *franciscanus* at least once before insemination occurred and no females were found inseminated until all traces of the blood meal were gone from the midgut. (In *A. m. fressborni* no relation could be found between blood-feeding of females and insemination.) Another point of interest mentioned is that both *boylii* and *franciscanus* types of eggs were produced from a single first generation, laboratory-reared, female *A. p. franciscanus*.

Four tables compare the rate of development of different generations of *fressborni*, the percentages of pupae obtained, the differences between field-collected and reared batches of mosquitoes and the hatchability of eggs of the various generations. H S Lesson

BATES, M. The Laboratory Colonization of *Anopheles darlingi*. J National Malaria Soc. 1947 Sept. v 8, No. 3 155-8.

When attempting to establish laboratory colonies of mosquitoes, techniques may have to be varied for different species, and though the author of this paper is not satisfied that he has discovered the most satisfactory methods of handling *Anopheles darlingi* he gives an outline of his present procedure, because it has served to maintain the colony for three months in his laboratory in Colombia.



For the culture medium, experience showed that best results were achieved with stream water and surface loam, with bread crumbs as larval food. To induce females to feed and mate, no special lighting arrangements had to be made and it was found that as a source of blood a calf was more convenient and satisfactory than either man or the other animals tried. For egg-laying females, dark dishes were more attractive than white ones, and the most suitable cage size was 2 metres high by 1.5 metres square, or larger.

*A. strodei* and *A. argyritarsis* were also successfully reared under the same conditions as *A. darlingi*, but attempts to rear *A. rangeli* and *A. pessoai* failed.  
H S Leeson

GIGLIOLI, G. Laboratory Colony of *Anopheles darlingi*. *J. National Malaria Soc.* 1947, Sept, v 6, No 3, 159-64, 1 fig.

In British Guiana, after an attempt to establish a laboratory colony of *Anopheles darlingi* had failed at the sixth generation, a second attempt was made and resulted in a colony which has now flourished uninterruptedly for over two years, and which by December, 1946, had passed through 35 generations.

Three cylindrical netting cages (60 cm high and 35 cm in diameter) have been found to be sufficient and more satisfactory than the usual wood, wire and glass cages. White china finger-bowls and larger white enamel basins are used for the aquatic stages. It was soon found that the selection of water was extremely important, the best results being obtained from clean fresh water with a pH of 6 or 7, the local artesian well water was excellent. For the females, feeds of human blood were offered every morning between 8 and 10 o'clock, no animals were used at all. Larval food consisted of a proprietary poultry mash, either plain or mixed with yeast. As the laboratory is situated among irrigated fields of cane and rice (the natural habitat of *A. darlingi*), no special arrangement had to be made to create suitable climatic conditions indoors; the only precautions necessary were to see that the colony was protected from draughts and excessive light. A table gives the average monthly temperatures and relative humidities in the laboratory, a temperature of 80°F and a relative humidity of 85 per cent may be regarded as optimal. A second table summarizes the duration of the periods of development for each stage from egg to adult for different seasons throughout thirty generations. There are, of course, certain extreme deviations, but apart from these there is a general tendency for certain values to recur irrespective of season. First ovipositions occur usually 6 to 8 days after emergence, eggs hatch in two days, the larval stage lasts 6 to 16 days and the pupal stage two days. The complete cycle can be accomplished in from 10 to 14 days. [Regarding the rearing of *Aedes aegypti* see JOHNSON, below.]  
H S Leeson

ALBERTO ALVARADO, C. & HEREDIA, R. L. Observaciones sobre una nueva variedad del *Anopheles* (*A. pseudopunctipennis* Theobald 1901, encontrada en la provincia de Tucuman (Nota previa). [A New Variety of *Anopheles pseudopunctipennis* in Tucuman]. *In: Inst. Med. Regional Tucuman Argentina* 1947 Nov. v 2, No 1, 73-8, 6 figs.

The English summary appended to the paper is as follows —

Using the morphological characteristics of the eggs as a basis the authors describe a new variety of *A. (A.) pseudopunctipennis* which they designate *p. personi*.

VILLALOBOS C. E. & VALDEERRAMA DELGADO A. *El Anopheles punctimaculatus* en el Perú. [1 *punctimaculatus* in Perú.] 12 pp. Lima, Dir. gen. Salub. Serv. nac. antimalar. 1944 [Summary taken from *Rev. Applied Entom.* Sér. B. 1947 Dec. v 35 Pt. 12, 204.]

Although *Anopheles punctimaculatus* D & L. had apparently not been recorded from Peru prior to 1942, it is now common in the district of Lima and is increasing. It constituted 80 per cent. of the Anophelinae taken in buildings in two localities in April-July 1944. Numerous breeding places occur in the coastal area, and in addition to the shaded and sometimes polluted water in which the larvae usually occur they have frequently been observed in still, clear sunny water together with those of *A. pseudopunctipennis* Theo. The importance of *A. punctimaculatus* as a vector of malaria has not been definitely established, but in the course of the authors' investigations, although dissection of about 1 000 females gave negative results, four of 135 taken in a house inhabited by two chronic malaria patients situated at a place some 13 miles from Lima, and two of 83 taken at a place 18 miles from Lima, showed sporozoites in the salivary glands. *A. pseudopunctipennis* is still considered to be the main vector however.

VON DRACHMANN J. Zur Frage der Wirkung des Hochgebirgsklimas beim Malariker. [On the Effect of Mountainous Climates on Malaria Patients.] *Acta Tropica*. Basle. 1947 v 4 No. 4 335-8.

The favourable effects of mountainous climates on malaria patients have not been satisfactorily explained says the author. By some it is ascribed to the general sense of well-being and consequent resistance to disease, by others to increase in red corpuscles and raising of the haemoglobin. Several other hypotheses have been put forward, such as changes in the fat and lipid ferments and vitamin A content of the serum. It is thought that a study of the reticulo-endothelial stage of the parasite may throw light on the subject.

On the other hand, malaria relapses are relatively common at mountain heights especially when there is a moist wind blowing. Further the endothelium is a tissue which readily responds to climatic changes and these reactions are rapidly set up when debilitated or sick persons reside at a height where moist south-west winds prevail.

The author suggests the following. The plasmodia under climatic influence do not enter the erythrocytes but remain, perhaps for months in the endothelium. At the same time the climate at high levels acting on the readily responding endothelium causes a flooding of the parasites into the blood-stream and so renders them more readily vulnerable to therapeutic measures. It is possible that in the endothelium especially the reticulo-endothelium at high levels, certain changes of a colloidal, histochemical, histophysiological or other nature might play a part in preventing penetration of the plasmodia into the corpuscles or in the development of endothelial forms. This solution of the question it is stated can at present only be suggested as research on it is completely wanting. [Not a very satisfying contribution and purely hypothetical.]  
H. Harold Scott

INVERNIZZI G. Osservazioni ematologiche mielografiche della malaria. [Haematology and the Myelogram in Malaria. *Rev. d. Malariologie* 1947 Oct. v 28 No. 5 234-47. [28 refs.]

The English summary appended to the paper is as follows:—

"The author carried out haematological investigation on 230 malaria patients. The method of haemochromocytometric examinations and myelograms by sternal puncture was used and he reached the following conclusions:

"1 In acute malaria the actual anaemia is not so severe as it appears from the clinical symptoms. The erythroblastic report [? findings] is scarce, and some myelocytes are found.

"2 In chronic splenomegalic malarial infection leucopenia with monocytosis is observed. During the stage of acute infection, with shivers, a moderate leucocytosis (7,500-8,000) was seen, with neutrocytosis (70-80%) and a reduction in eosinophiles. As the temperature falls leucopenia returns (3,500-5,000) with neutropenia, mononucleosis and lymphocytosis. Mononucleosis and deviation of the Arneth count to the left are constant.

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VAN DER KUYP, E. De pols en ademhalingsfrequentie bij malaria. [The Pulse and Respiration Rates in Malaria] Reprinted from *Nederl Tijdschr v Geneesk* 1947, Mar 29, v 91, No 13, 735-9. English summary.

The author studied the relation between temperature, pulse and respiration in several patients suffering from the three main forms of malaria. 130 of them suffered from quartan infections, mostly of a chronic type.

Although the three factors sometimes corresponded sufficiently with the type of infection, the pulse and respiration curves appeared to be more sensitive indications than the temperature of the progress of the disease during treatment, since they became normal later than it, a prolongation of their abnormality is stated to have heralded relapses and even the initial attack could sometimes be anticipated by their variations. Hourly readings made these observations more pronounced.

It is suggested that as a result of "schizogony on a small scale," the amount of toxin released is too small to influence the temperature, but that the pulse and respiration are more sensitive to those toxins.

H J O'D Burke-Gaffney

CALEY, F E de W. Clinical Impressions of Malaria and Liver Damage. [Correspondence] *Lancet* 1947, Dec 20, 926-7.

The paper by MAEGRAITH, ANDREWS and GALL [see this *Bulletin*, 1948, v 45, 234] reminds the author of cases of malaria with liver damage seen by him in Siam. He states that 400 men, being prisoners of war, were working on the Mergin road from May to August, 1945. Of these 100 died and half of them died in an unusual manner. The illness began with continuous fever of about 102°F. After 5 days, hiccup began and the patients became deeply jaundiced. After four more days, they became comatose, with stertorous breathing suggestive of hepatic failure and with hiccup after every few respirations. Three days later death occurred. Vomiting was present but was not severe, while complete anorexia occurred. There was no tendency to haematuria or general haemorrhage. The urine was scanty and coloured by bile pigment. There was some enlargement of the spleen and liver. Later, some of the patients were evacuated to Nakon Paton. The author heard that the blood slides showed *Plasmodium falciparum*. It is suggested that these cases were due to a hepatotoxic strain of this parasite. They did not resemble bilious remittent fever, which was not encountered. At another camp in Siam, there was a higher incidence of cerebral malaria than elsewhere. It seemed possible that the strain of *P. falciparum* was of an encephalopathic type. Blackwater fever

VILLALOBOS C. E. & VALDERRAMA DELGADO A. El *Anopheles punctimacula* en el Perú. [*Anopheles punctimacula* in Peru.] 12 pp. Lima, Div. gen. Salub., Serv. nac. antimalar. 1944 [Summary taken from *Rev. Applied Entom.* Sér. B. 1947 Dec., v 33 Pt. 12, 204]

Although *Anopheles punctimacula* D & L. had apparently not been recorded from Peru prior to 1944, it is now common in the district of Lima and is increasing. It constituted 80 per cent. of the Anophelines taken in buildings in two localities in April-July 1944. Numerous breeding places occur in the coastal area, and in addition to the shaded and sometimes polluted water in which the larvae usually occur they have frequently been observed in still, clear sunny water together with those of *A. pseudopunctipennis* Theo. The importance of *A. punctimacula* as a vector of malaria has not been definitely established, but in the course of the authors' investigations although dissection of about 1 000 females gave negative results, four of 135 taken in a house inhabited by two chronic malaria patients situated at a place some 13 miles from Lima, and two of 93 taken at a place 18 miles from Lima, showed sporozoites in the salivary glands. *A. pseudopunctipennis* is still considered to be the main vector however.

VON DESCHWANDEN J. Zur Frage der Wirkung des Hochgebirgsklimas beim Malariker. [On the Effect of Mountainous Climates on Malaria Patients.] *Acta Tropica*, Basle. 1947 4 No. 4 335-8.

The favourable effects of mountainous climates on malaria patients have not been satisfactorily explained, says the author. By some it is ascribed to the general sense of well-being and consequent resistance to disease by others to increase in red corpuscles and raising of the haemoglobin. Several other hypotheses have been put forward, such as changes in the fat and lipoid ferments and vitamin A content of the serum. It is thought that a study of the reticulo-endothelial stage of the parasite may throw light on the subject.

On the other hand, malaria relapses are relatively common at mountain heights especially when there is a moist wind blowing. Further the endothelium is a tissue which readily responds to climatic changes and these reactions are rapidly set up when debilitated or sick persons reside at a height where moist south-west winds prevail.

The author suggests the following. The plasmodia under climatic influence do not enter the erythrocytes but remain perhaps for months, in the endothelium. At the same time the climate at high levels acting on the readily responding endothelium causes a flooding of the parasites into the blood-stream and so renders them more readily vulnerable to therapeutic measures. It is possible that in the endothelium especially the reticulo-endothelium at high levels, certain changes of a colloidal, histochemical, histophysiological or other nature might play a part in preventing penetration of the plasmodia into the corpuscles or in the development of endothelial forms. This solution of the question it is stated can at present only be suggested as research on it is completely wanting. [Not a very satisfying contribution and purely hypothetical.]  
H. Harold Scott

INVERNIZZI G. Osservazioni ematologiche e mielografiche della malaria. [Haematology and the Myelogram in Malaria.] *Riv. di Malarologia* 1947 Oct. v 28 No. 5 234-47 [28 refs]

The English summary appended to the paper is as follows —

"The author carried out haematological investigation on 230 malaria patients. The method of haemochromocytometric examinations and myelograms by sternal puncture was used and he reached the following conclusions

" 1 In acute malaria the actual anaemia is not so severe as it appears from the clinical symptoms. The erythroblastic report [? findings] is scarce, and some myelocytes are found.

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was sporadic in incidence—one in four of the patients died. Treatment was by intravenous mepacrine. Where dysentery occurred with malaria, it was the interaction of two diseases. \ cases of choleraic, algid, cardiac or purpuric type were seen. Three cases were seen which resembled acute haemolytic anaemia with air hunger and a lemon-yellow skin and conjunctivae, without haemoglobinuria.

C. M. Wenyon

HERNBERG C. A. Malaria Tertiana and Renal Injury *Acta Med Scandinavica*. 1947 Sept. 22, v 128 No. 6, 590-65. [12 refs.]

This paper contains a short account of four cases of malignant tertian malaria occurring in Finland, showing signs of renal disturbance. In three, the renal damage was of the character of focal nephritis. The kidney syndromes in all cases were relieved by antimalarial treatment. A short note is given of the literature on the subject of renal damage in malaria, especially damage to the tubular epithelium in malignant tertian evidenced by dilution of urine, diminution in output and rise of blood non-protein nitrogen. The four cases referred to in the text are the only cases with renal symptoms in 1,500 cases reported over the years 1941-45.

B. G. Macgregor

BENHAMOU E. ALBOU A. ZERMATI M. & EISENBATH R. Hémorragie méningée au cours d'un paludisme à *Plasmodium vivax*. Considérations pathogéniques. [Haemorrhagic Meningitis during *Plasmodium vivax* Malaria.] *Algérie Méd.* 1947 Oct v 50 No. 8, 611-14

Haemorrhagic manifestations appear to be rare in malaria—the authors quote SERRAER and KRAM (this *Bulletin* 1947 v 44 170) who met only 10 cases of purpura in 10 000 consecutive cases of malaria treated in Panama—none of the published cases noted by these authors included meningeal lesions.

The present case refers to an Algerian who complained of persistent headaches for five days accompanied by vertigo. Although he had a history of trauma on two occasions (one involving the neck seven years earlier) these accidents were not serious and could not be regarded as relevant to the present condition. For nine months, the patient had felt weak and experienced fever of a malarial type almost daily—he noticed a swelling of the abdomen and an intermittent discomfort in the left hypochondrium.

On examination, he looked thin with pale conjunctivae—the spleen was considerably enlarged, but painless. Lumbar puncture produced a reddish fluid, which did not coagulate on standing and which showed no micro-organisms on direct examination. Two blood films taken after an interval of 3 days, showed the presence of *Plasmodium vivax*. Haematological examinations revealed a normocytic, normochromic anaemia, with 2,300 000 red corpuscles per cmm. and 51 per cent. reticulocytes—cold agglutinins were present at a titre of 1/32.

The bleeding and coagulation times and the platelet count were as follows—

	1st day	9th day	29th day	36th day
Bleeding time	15	3' 30"	3'	4-45
Coagulation time	8"	4	12"	8"
Platelet count	44 000	77 000	100 000	133 000

The haemorrhagic and meningeal syndromes both responded to quinine and the cerebrospinal fluid was normal on the 30th day

The authors refer to the literature of purpura in malaria [see this *Bulletin*, 1938, v 35, 728] and quote cases in which haemorrhages in different organs had been noted but none of these included the meninges, nor were they related to any one species of *Plasmodium* only

In Shrager and Kean's cases [and in that recently reported by MAMOU [this *Bulletin*, 1948, v 45, 237] the purpura followed on administration of quinine in 9 of the 10 cases in the present case, no such treatment had been given before the onset of the haemorrhagic condition

In discussing the pathogenesis of the condition, the authors quote BENHAMOU and NOUCHI (*C R Assoc française pour l'avancement des Sciences Algér* 1930, May), as having shown a significant decrease in platelets in malaria they also refer to a thesis, published in Algiers by ASSUS in 1945, which suggests that haemorrhagic manifestations are not uncommon in patients having a raised titre of cold agglutinins. The authors therefore conclude by posing the question: What complementary rôle may auto-agglutinins play in the appearance of haemorrhages during malaria? H J O'D Burke-Gaffney

WINCKEL, C W F Quinine and Congenital Injuries of Ear and Eye of the Foetus *J Trop Med & Hyg* 1948, Jan, v 51, No 1, 2-7, 3 maps [13 refs]

It is well known that temporary deafness or blindness may occur as a result of quinine intoxication

The author draws attention to 15 instances of congenital deafness and two of congenital blindness described in the literature as occurring in cases where the mother has taken quinine in pregnancy or just before labour. All these cases were noted in the United States of America, and the amount of quinine taken varied from quite small to large doses. In one instance, the mother had been given 90 grains daily, by mouth and injection, for 7 weeks during pregnancy, the child was deaf for 6 months after birth, but ultimately recovered and at the end of 17 months hearing was perfectly normal. [As the author remarks it is a wonder, if this statement is true, that the patient survived.] It was found that the auditory and visual defects were not influenced by the amount of quinine taken

The cases described are very few, only 17 appearing in the literature and all from the United States, yet the world consumption of quinine is estimated at from 600,000 to 800,000 kilogrammes yearly. If quinine is an important cause of congenital deafness or visual defects, cases would surely have been met with and reported more frequently and from all malarious parts of the world. Further, there is no correlation between the endemic incidence of malaria in the various States and the proportion of their inhabitants who are deaf mute or blind. This is clearly shown in 3 maps which give (a) the endemic malarious areas in various States, (b) the ratio of deaf mutes, (c) the ratio of blind persons in various States

It is of interest to note that several series of such congenital auditory and visual defects have been described in instances where the mother has suffered from rubella in pregnancy [see *Bulletin of Hygiene*, 1947, v 22, 172, 390]

[The reviewer has attended several hundred confinements in malarious districts among the non-indigenous population, most of whom had taken quinine at some time during pregnancy. In only one case was a case of deaf-mutism seen, the mother, a European, having taken 5 grains of quinine daily during almost the whole of pregnancy. The child subsequently turned out to be mentally defective and it is not thought that quinine can be blamed for the condition. It would be interesting to know whether a daily prophylactic dose of quinine taken over the course of years predisposes to deafness]

C F Shelton

PLOTT M. Quick aspects de la question des Totaguinas. (Some Aspects of the Totaguina Question.) *Rev. Paludisme et Méd. Trop.* 1948, Jan. 15. 6  
No. 44 1 17 (Ref. in footnotes.)

MACHELLA T. E., KIRKELMAN L. J. & LEWIS R. A. The Intravenous Administration of Atabrine in Falciparum Malaria. *Bull. U.S. Army, Med. Dept.* 1947 Dec. v 7 No. 12, 1009-21

Many authorities regard the intravenous use of atabrine (mepacrine) as dangerous. This paper is the result of observations on 125 Chinese soldiers treated in Burma during the active malaria season (June-October 1944) and a series of experiments was planned to learn how this drug could be given most safely by the intravenous route.

No attempt was made to select cases but those with severe cerebral symptoms received the larger doses. All cases in this series had positive blood films.

The degree of parasitaemia was graded as follows (1) rare to few (2) moderate (3) many (4) loaded.

The following schedules were used —

Intravenous atabrine 0.4 to 1 gm. of the dihydrochloride was dissolved in distilled water (0.2 gm. in 10 c.c.) and this solution was added to 1,000 cc. of normal saline and given by intravenous drip over a period of 3-4 hours.

Quinine the dihydrochloride (1.2 to 2 gm.) was dissolved in 30 to 50 cc. of distilled water and the solution was added to 1,000 cc. of normal saline and given by intravenous drip.

S.N. 6911 besulphate (a 4-amino quinoline derivative) 0.64 gm. was dissolved in 1,000 cc. of normal saline and given by intravenous drip.

Atabrine by mouth 0.2 gm. of the dihydrochloride was given every six hours for five doses and then 0.1 gm. thrice daily for six days.

Daily thick blood films were examined until two negative smears were obtained.

The results of treatment may be summarized as follows —

1. Atabrine by mouth (2.8 gm. in 7 days) 20 cases. The average duration of fever after beginning treatment was 45.6 hours. Blood films were negative on an average 3 days after beginning treatment. All cases responded to treatment and there were no toxic reactions.

2. Quinine (1.2 gm. intravenously) 10 cases. The average duration of fever was 45.6 hours in the cases where the attack was terminated by the single injection and blood films were negative after 3.2 days. No toxic reactions were experienced but in five patients the single injection failed to terminate the attack and additional antimalarial therapy had to be given. [The nature of the further treatment is not mentioned.] A single infusion of 2 gm. given to 3 patients produced alarming collapse and was discontinued.

3. Atabrine (0.4 gm. intravenously) 10 cases. The average duration of fever was 21.8 hours. Blood was negative after 2.3 days. No toxic reactions were observed, but in one case this treatment did not stop the attack.

4. Atabrine (0.8 gm. intravenously) 20 cases. Average duration of fever 29.1 hours, negative smear after 2.3 days. No toxic results followed and all cases responded.

5. Atabrine (0.8 gm. intravenously) 20 cases. Average duration of fever 24.2 hours, films negative after 2 days. All responded to treatment and there were no toxic reactions.

6. Atabrine (1.0 gm. intravenously) 23 cases. Average duration of fever 31.6 hours. Blood negative after 2.2 days. All cases responded, but in two instances mental symptoms of a temporary nature occurred, namely excitement, exhilaration and in one case a short generalized convulsion. Through an error the first of these patients had received his injection in 50 minutes.



7 S N 6911 (0.64 gm intravenously) 20 cases Average duration of fever 41 hours, blood negative in 25 days No toxic signs were noted and all reacted to the dose given

Eight of the 125 patients showed severe cerebral signs with coma, four of these being treated with 0.8 gm and four with 1.0 gm of atabrine intravenously, all with success No mention is made of the cerebral conditions in the remaining cases It may be noted that in half the cases so treated, a single infusion of intravenous quinine failed to control the attack Three cases of *P. vivax* infections were treated with 2.0 gm quinine intravenously, all three showing severe collapse shortly after the injection

Serum atabrine concentrations were determined by a field method [see this *Bulletin*, 1945, v 42, 443]

A factor which appeared to determine the serum atabrine level was the rate at which the injection was given, for a given dose a higher concentration was found when the injection was given rapidly The concentration tended to be highest at the end of the injection, varying from 200 to 540 microgrammes per litre except in one case where a concentration of 1,100  $\mu$ gm was found without detectable toxic symptoms After cessation of treatment the amount steadily decreased to an average of 20  $\mu$ gm per litre on the 5th day, although small amounts were found as late as the 3rd week

The authors conclude that —

1 Intravenous atabrine in dilute solution, i.e., in 1,000 cc of normal saline, is well tolerated, and amounts up to 1.0 gm can be given safely

2 The drug should be administered by the drip method over a period of 3 to 4 hours

3 Toxic manifestations are negligible where proper precautions are taken

There were no deaths in this series

The authors emphasize the fact that they do not suggest that the injection of this drug should be generally adopted as a routine method of treatment

RAO A. R. G. A Case of Maniacal Excitement following Large Dose of Atabrine  
*Indian Med Gaz* 1947 Aug v 82 No 8 479-80

MACKERRAS, M. J. & ERCOLE, Q. N. Observations on the Action of Atabrine on Malarial Parasites  
*Trans Roy Soc Trop Med & Hyg* 1947 v 41, No 3, 365-76, 1 coloured pl & 1 graph

The changes which the sexual and asexual forms of human malarial parasites undergo during the development cycle in man have been carefully studied by the use of stained blood films of the untreated host and at various intervals after treatment of paludrine The development of the parasites in the mosquito has also been studied. Some of the observed facts have been briefly summarized by FAIRLEY [this *Bulletin*, 1947, v 44, 282] In the case of *P. vivax* it was found that the drug exerts its lethal action on the dividing nucleus of early schizonts and that growth occurs normally up to this point Gametocytes are visibly affected. Fertilization occurs in the mosquito stomach, but cysts do not mature and the mosquito gut infection becomes sterilized Gametocytes of *P. falciparum* likewise developed normally in blood, and reached the stage of encystment in the mosquito gut, but further development was inhibited and the infection in this case was also sterilized if a sufficient amount of drug had been present in the host blood Gametocytes which survived some 12 days after treatment of the host was discontinued, developed normally in mosquitoes, but traces of paludrine in the blood, sufficient at 10 days to affect development, had apparently disappeared by the 12th day In the case of *P. malariae* the action

PLORA, M. Quelques aspects de la question des Totagumas. [Some Aspects of the Totaguma Question.] *Rev. Parasitisme et Méd. Trop.* 1948, Jan. 15 6  
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6. Atabrine (1.0 gm. intravenously) 25 cases. Average duration of fever 4 hours. Blood negative after 2.2 days. All cases responded, but in two instances mental symptoms of a temporary nature occurred, namely excitement, exhilaration, and in one case a short generalized convulsion. Through error the first of these patients had received his injection in 50 minutes.

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of the drug was on young schizonts but the parasite appeared to be more resistant than *P. vivax*. There is an excellent coloured plate depicting the changes brought about by paludrine on the asexual forms of the latter parasite.  
J. D. Fulton

SEW A. Treatment of Malaria with the New Synthetic Drug "Paludrine"  
Calc. & Med. J. 1947 July v 41 No. 7 170-74

A report of 7 cases, with successful clinical results.

KIKER C. G. & MARRIS P. Aerial Mapping in Malaria Control. J. National Malaria Soc. 1947 Dec. v 8 No. 4, 219-23, 6 figs.

JOHNSON C. G. & WALTON W. H. The Effect of Area Dosage, Solution Concentration and Drop Size of Sprayed Solutions and Emulsions of DDT against Mosquito Larvae. Bull. Entom. Res. 1947 Dec. v 38, Pt. 3 405-30 15 figs. & 4 pls.

This account describes war time experiments on a strip of mosquito-infested canal in Surrey about 1 100 yds. long and 40 ft. wide. The mosquitoes were mainly *Anopheles maculipennis* (meagles) with a few *A. claviger*. The canal was a disused section with no water flow the centre carried patches of floating vegetation and the margins were fairly densely grown with reeds. Sections 20 ft. long and at least 40 ft. apart were chosen for the experimental areas. The applications were made by an ingenious machine which distributed the spray drops from a rapidly spinning disc this was moved backwards and forwards across the canal on a wire, thus treating the water in strips. The droplet size could be altered by varying the disc size and the rate of delivery was controlled by varying the liquid feed on to the centre of the disc. For uniform distribution, an eccentric disc with a spiral edge was most satisfactory. Estimation of results was made by regular dipping at intervals and at different distances from the bank all along one side of the canal. These dippings were made for several days before and for about a month after spraying.

The first experiment was made to determine the minimum lethal dose of DDT in an emulsion at 0.5 per cent. with droplets about 0.4 mm. diameter. The emulsion AMSO was made up from the following concentrate: 30 gm. pure DDT 400 ml. pool 3 oil, 200 ml. Amcol A5A (an emulsifier mainly sodium oleate and cresol).

The second experiment was designed to compare DDT in oil (5 per cent. solution aided by solvent naphtha as an auxiliary solvent and oleic acid as a spreader) with the emulsion used in the first test.

The third experiment was to test the effects of droplet size.

The fourth experiment investigated the effects of dilution on oil solutions containing the same amounts of DDT per unit area.

Results —

1. The critical density of application appeared to be about 40 gm. DDT per acre (10 mgm. per sq metre). Doses above this were not economically more efficient and doses below gave unreliable results, especially in water among reeds.

2. The oil solution gave results definitely superior to the emulsion, especially among the reeds at the edges of the canal.

3. The finer droplets tended to be blown away from the experimental plots and thereby these tests were handicapped. But where due allowance was made for this by estimating the quantities actually falling on the water there was no difference in efficiency between drops of 0.4 mm. diameter and of 1 mm. diameter.

4 Dilution of 4.3 per cent DDT in oil ten times (i.e., 0.43 per cent) gave almost the same, or slightly inferior, results where the actual quantity of DDT delivered to the water surface was kept constant J R Busvine

KUCHER, S S Testing Insecticidal Properties of the Preparation "Insectol" on Mosquitoes *Vrachebnoye delo* 1946, No 5, 245-6 [Summary taken from *Amer Rev Soviet Med* 1947, Dec-1948, Jan, v 5, No 1, p 70 Signed Otto HOKE]

"Insectol is a complex mixture of aromatic carbohydrates and sulphonaphtholic acids. The basic material for its production is the light medium coal tar oil, which is obtained as a by-product in rectification of coal tar. Mixed with water, in which it is highly soluble, it forms a milky emulsion. Its insecticide effect on *Anopheles maculipennis* was tested in laboratory experiments with 3, 4, 5, 10 and 20 per cent solutions. It was found that 40 cc of a 10 per cent emulsion, sprayed on one square meter of a floor or wall of a barn, killed 98 per cent of the mosquitoes within one hour. The same result was obtained with 20 cc of a 20 per cent emulsion. While these results applied to spraying in the open, the toxicity of insectol was found to be far higher when used in stalls and chicken pens. It was proved that insectol acted upon the mosquitoes by mere contact.

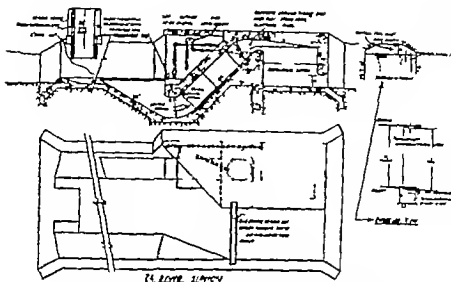
"For practical use 15 per cent emulsions are manufactured. The spraying of walls outside and inside buildings with 30 cc of this emulsion per square meter yields satisfactory results. For tightly closed rooms a 10 per cent emulsion suffices. The odor from spraying with the preparation evaporates after ventilation for five to six days. The unpleasant odor prohibits the use of insectol in human habitations."

PEREDO REYES E El cultivo del arroz y sus relaciones con el paludismo en el Estado de Morelos [Rice-growing and its relation to Malaria in the State of Morelos] *Rev Soc Mex Hist Nat* 1945 v 6 Nos 3/4 161-78 4 pls & 3 graphs

NEWBOLD, C E & COCHRANE, E Automatic Siphons for Antimalarial Control of Tropical Streams *J. National Malaria Soc* 1947, Sept, v 6, No 3, 192-205, 4 figs & 3 charts

Mechanical fluctuation and turbulence of streams in the wet season in the West Indies is believed to be responsible for the absence of the coastal anopheline, *Anopheles aquasalis*, which usually invades such streams in the dry season from the brackish coastal swamps.

A steady flow of water throughout the dry season permits the use of automatic siphons to produce the necessary flushing and turbulence. The authors consider that control of anopheline breeding is effected by damage to and stranding of eggs. Various types of siphons had been constructed previously without completely satisfactory control of breeding because of technical inefficiency of the automatic siphons. As a result of experience gained, a siphon (deep seal) of 24-inch diameter was built with simple but carefully designed automatic control devices. The best materials and workmanship were necessary to obtain a well-constructed supply reservoir with siphon in order to minimize maintenance costs, labour being expensive in Trinidad. For this particular siphon, a catchment area of 1 000 acres in the dry season enabled sufficient water to be impounded to produce an average discharge for ten minutes at the rate of 20 cubic feet per second, or about 70,000 gallons of water. The six-foot-wide stream was raised 17 inches at 2,000 feet, 13 inches at 6,000



Working design for 34-inch siphon for the control of mosquito breeding in tropical streams.

[Reproduced from the *Journal of the National Malaria Society*]

feet and 4 inches at 10,650 feet downstream the wave took 80 minutes to reach the last point. Complete anopheline control was attained during six months observation. In comparison, Ramsay in northern Bengal [this *Bullet* n 1941 v 38, 232] considered a total discharge of 50,000 gallons was the minimum amount necessary to control a mile channel (5,280 ft) 8 to 8 feet wide.

It is not possible to summarize the discussion and constructional detail given in this most useful paper but the appended working design will be helpful to those interested. To promote smoothness of action the authors have incorporated a 1 inch control siphon and an adjustable top to the control seal. Malaria engineers are strongly recommended to refer to the original paper with its clear diagrams and excellent photographs.

R. Ford Trede

STAGE, H. H. & GIGLIOLI, G. Observations on Mosquito and Malaria Control in the Caribbean Area. Part II. British Guiana. *Mosquito News*. 1947 June v 7 No. 2, 73-8 2 figs.

The authors are of opinion that there are probably few countries where malaria constitutes a more serious problem than in British Guiana. In a population of 350,000 deaths ascribed to malaria are two per thousand inhabitants per annum—a much larger number of deaths due to anaemia, nephritis, prematurity and debility in infants are caused indirectly by repeated malaria infections—dangerous forms of the disease are frequent.

The inhabitants of the alluvial coastal zone, mixture of Negroes, Chinese, Portuguese and East Indians, accept malaria as inevitable. Filariasis is also a major problem and yellow fever a permanent potential danger.

The staple crops, rice and sugar cane, are dependent on extensive irrigation systems despite an annual rainfall of 80 inches. Much of the rice and cane fields along the coast are below high tide level and the practice of flooding fields, and the maze of irrigation channels provide most favourable conditions for

anopheline breeding There are fifteen anopheline species, mainly zoophilous, the principal exception being *A. darlingi*, which bites man for preference and is found in houses in large numbers before and after biting

On the coastal zone, *A. darlingi* breeds in large areas of fresh water such as canals and rice and cane fields In the interior, it prefers the clear water of ponds, lakes and streams Salinity and acidity of waters limit its distribution

*A. aquasalis* and *A. oswaldoi*, which breed in saline waters, do not appear to be efficient vectors of malaria

The ten years' observation by Giglioli indicate that sea defences, irrigation and associated cultivations, when used without discrimination between agricultural and residential lands, bring about the establishment of *A. darlingi* and subsequently endemic malaria

Experience has shown that DDT applied as a residual insecticide is most effective against the vectors of malaria, yellow fever and filariasis, namely *A. darlingi*, *Aedes aegypti* and *Culex fatigans* to the extent that they are "in grave danger of extermination" The cost is not excessive, amounting to slightly less than one dollar (British Guiana), per 1,000 square feet of surface treated

R Ford Tredre -

GRAY, H F Mosquito Control Problems in Japan *Mosquito News* 1947, Mar, v 7, No 1, 7-11

Japan is infested with mosquitoes to the extent that people are so inured to insect attack as to be more or less indifferent to their presence

Ricefields produce the malaria vector, *Anopheles hyrcanus sinensis*, and the presumed and probable vector of Japanese B encephalitis *Culex tritaeniorhynchus* Cost prevents the use of larvicides, "intermittent drying in predetermined cycles" and the introduction of larvicidal fish are recommended to the government as effective and inexpensive control measures, where outbreaks of disease occur these measures may be supplemented by larvicides and residual insecticides

Water containers produce the vector of dengue, *Aedes albopictus* and *Aedes togoi* Epidemic dengue occurred between 1942 and 1944, an important contributory factor being *Aedes* breeding in the household concrete water-containers introduced for fire-control purposes Small containers in cemeteries are also notable breeding places

In the rural areas and unsewered portions of cities, human excrement is kept for fertilizer purposes in liquid manure tanks, *Culex pipiens pallens* and *Armigeres obturbans* breed profusely in these and other collections of foul water

Reasonable reduction in numbers of mosquitoes can be readily attained at very moderate expense *Anopheles hyrcanus sinensis* has a marked preference for large animals, and is effective as a malaria vector only if it is present in enormous numbers

Ignorance and indifference on the part of an impoverished population must be overcome by education before mosquito control measures can be effectively applied

[The co-author of the well-known text book on Mosquito Control methods has given a useful concise account of mosquito infestation in post-war Japan from the point of view of the military forces of occupation]

R Ford Tredre

JOHNSON, H A Practical Laboratory Methods for Quantity Rearing and Handling of *Aedes aegypti* Mosquitoes to be infected with *Plasmodium gallinaceum* *J National Malaria Soc* 1947, Sept, v 6, No 3, 173-9, 4 figs

The methods of rearing *Aedes aegypti* described in this paper have been developed over a period of two years in connexion with studies of *Plasmodium gallinaceum* in chickens

The mosquito colonies are kept at about 75°F and at a relative humidity between 70 and 75 per cent. The cages are made of wire screening on 3-foot cubical frames with a front of glass having a 18-inch square opening fitted with a sleeve. A partially shaved rabbit provides the blood meal and 5 per cent. sugar water is kept in the cages. Eggs are laid on wet cellulose sponges these are removed every second day kept wet for 72 hours and then dried. The dried sponges may be stored for as long as two months to build up a reserve of eggs. After the sponges are immersed, hatching of the eggs is completed in 36 hours and the young larvae are removed to rearing pans and fed on ground Pabulum. Pupae develop in 6 to 10 days and the production is about 2,000 per day. Of these 800 female pupae are picked out for experiment and the remainder returned to the colony. The 800 pupae are placed in bowls (100 to a bowl) under lamp chimneys with bobbinet tops. 50 to 75 adults usually emerge from each 100 pupae in 1 to 3 days and the chimneys are then removed to the feeding room. Here they are clamped to platforms over one-inch holes which are closed with two thicknesses of rubber having cross slits through which the insects may be removed with a suction tube. Wet cotton is kept on the bobbinet for three days. Next day a chicken is placed across the bobbinet top and held by a cloth wrapping and rubber bands. About 50 to 90 per cent. of the mosquitoes feed in half an hour and the gorged females are removed to a fresh chimney on which is a cotton pledget soaked in 5 per cent. sucrose. After 10 days, a few mosquitoes are examined for sporozoites and sporozoite inoculations are usually prepared from the 12th to the 15th day.

Unused females are kept until they die and some have lived for 110 days though usually only 5 to 30 per cent. survive after a month.

H S Lacey

HAAS V H & AKINS H. Transmission of *Plasmodium gallinaceum* by *Anopheles quadrimaculatus*. *J National Malaria Soc.* 1947 Dec. v 6 No. 4 244-5.

*Plasmodium gallinaceum* has been successfully transmitted by at least 27 species of mosquitoes (belonging to five genera—*Aedes*, *Armigeres*, *Culiseta*, *Mansonia* and *Theobaldia*).

These authors report success for the first time with the use of an anopheline mosquito *A. quadrimaculatus*. The mosquitoes were obtained from a long established colony and were allowed to bite chicks whose blood contained gametocytes of *P. gallinaceum*. The insects were kept at 74-76°F in a relative humidity of 70 per cent. After 10 days, three stomachs out of ten showed oocysts; after 12 days eight in 13 were positive. Seven of the latter were heavy infections and exhibited ripe sporozoites—later shown to be infective by inoculation into chicks, one of which developed parasites. On the fourteenth day the infection was successfully transmitted by biting (1 chick in 3 showing a patent infection) and also in a separate test by inoculation of the triturated mosquitoes in serum saline.

The authors state that mosquito dissections do not have to be interpreted with care, because they may represent avian rather than human infections. In many parts of the world this would be unnecessary either because the known anopheline vectors are purely anthropophilic in their habits (and thus unlikely to bite the wild birds) or pre-emptive entomological tests have already proved that their stomach contents do not contain a malarial parasite. In doubtful cases it is a simple matter to examine the blood in the stomach of the suspect species and see if it consists of nucleated corpuscles or not.

P C C Garahan



BECKMAN H Attempted Infection of the Hen and Man with the Sporozoites of *Plasmodium cathemerium* 3H2 *Proc Soc Exper Biol & Med* 1947, Nov, v 66 No 2 401-2

The trials were not successful

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## BLACKWATER FEVER

RAOULT A Un cas d'anurie prolongée au cours d'une fièvre bilieuse hémoglobino-urique [A Case of Prolonged Anuria during Blackwater Fever] *Bull Méd del Afrique Occidentale Française* 1947, v 4, No 1, 43-8 1 folding chart

BURWELL, E L, KINNEY, T D & FINCH, C A Renal Damage following Intravascular Hemolysis *New England J of Med* 1947, Oct 30, v 237, No 18, 657-65, 5 figs [43 refs]

This paper is essentially a case report on a 29-year old woman admitted to hospital because of anuria following abortion and subsequent massive intravascular haemolysis. Three months after this episode, the patient died of homologous serum hepatitis. Autopsy afforded a unique opportunity to examine residual anatomical lesions in the kidneys three months after the anuric attack.

The kidneys were of normal size and shape, the capsules stripped readily, the surfaces were pale brown and firmly granular. The ratio of cortex to medulla was normal. Histologically, there was diffuse sub-capsular scarring with narrow bands extending deep into the medulla. There was some oedema of the interstitial tissue and focal collections of lymphocytes in the scarred areas. Most of the glomeruli were normal in appearance, but in the scarred areas there was some pericapsular scarring. Some of the convoluted and more particularly the collecting tubules, especially those in the outer zone, were dilated and the lining epithelium flattened. A few tubules contained hyaline casts, and sometimes desquamated epithelial cells. According to the authors, the pattern was such as to suggest the destruction of a single nephron or a group of nephrons.

The nature of the haemolytic reaction in this case was not discovered.

There is a discussion on haemoglobinuric nephrosis and its pathogenesis in general. The authors conclude that no one factor is solely responsible. The therapy of haemoglobinuric nephrosis is also discussed in relation to the case described. The authors stress that in the stage of haemoglobinuria and subsequent anuria the maintenance of blood volume and renal blood flow and a controlled fluid intake should be aimed at.

[As a clinical case report, this paper is interesting. It should have been confined to this. There is nothing new in the discussion on haemoglobinuric nephrosis. Reference to a great deal of relevant literature is omitted. For example the statement is made that "immediate alkalization is indicated in spite of the conflicting experimental evidence regarding its effects". In support of this dogmatic advice, with which the reviewer heartily disagrees, the reader is referred to one paper only, published in 1940. Work subsequent to this has been ignored.]

B G Maegraith

# TRYPANOSOMIASIS

PELLERIN, A. Particularités morphologiques des pièces génitales de *Glossina palpalis* Robinson Desvoidy et de *Glossina palpalis* Rob. Desv. var *fuscipes* Newstead, et de *Glossina tachinoides* Westwood, en Afrique Equatoriale Française. [Morphological Features in the Genital Organs of *G. palpalis* *G. palpalis* var *fuscipes* and *G. tachinoides* in French Equatorial Africa.] *Bull. Soc. Path. Exot.* 1947 v 40 Nos. 8/10 335-81 5 figs.

HOLLIS, C. Streaky Blood Films. [Correspondence.] *Lancet* 1947 Dec. 20 828.

The author refers to a paper by BOWEN *et al* (*Lancet* 1947 Dec. 6, 831) in which it is stated that the streakiness in blood films gives a useful clinical indication of the plasma fibrinogen level, and, in most cases, of the corrected erythrocyte sedimentation rate.

The present author noted that in the blood of Africans with *Tryp gambiense* infections, the plasma albumin-globulin ratio is usually reversed, there is intense rouleaux formation and the blood sedimentation rate is much increased. With whole citrated blood, the B.S.R. did not change when it was repeated after re-mixing one hour later. If defibrinated blood was used (with or without citrate) the first B.S.R. was only slightly below that of the whole blood, yet on re-mixing after one hour both sedimentation and rouleaux formation had entirely disappeared. These results were obtained alike at blood temperature and at 0°C.

The author found one part of a 10 per cent. solution of suramin to 4 parts of blood to be an excellent anticoagulant which also inhibits rouleaux formation and sedimentation. It is suggested that these properties might have practical uses in haematology. *H. J. O'D. Burke-Gaffney*

SCHULZ, A. L'aspect des maladies tropicales en Suisse. Deux cas de trypanosomiase humaine africaine. [Two Cases of African Trypanosomiasis contracted in Switzerland.] *Acta Tropica*. Basle. 1947 v 4 No. 4 298-311

This is a detailed record of two cases of accidental *T. gambiense* infections in laboratory workers at the Swiss Tropical Institute in Basle. The subjects were women aged 27 and 22, respectively and the infecting strains had been brought to Switzerland from Léopoldville and Brazzaville in 1945. One of them was arsenic-resistant. The earlier history of these strains is not given.

The patients were apparently infected not by accidental inoculation but by contaminating their fingers with infected blood, in the course of transmitting the strains through guinea-pigs. The onset in the first case was by a sharp attack of fever with headache followed by lassitude, insomnia, anorexia and an eruption of non-infiltrated, non-pruriginous erythematous spots on the skin of the abdomen. Trypanosomes were found in the blood 3-4 weeks after the onset of fever.

The second patient's illness began also with headache and fever lasting about a week, which then subsided for a month, but reappeared with headache and lassitude. Trypanosomes were found in the blood about two months after the beginning of the illness, by which time an eruption similar to that of the first patient had appeared on the abdomen.

Both patients were treated by combined atoxyl and tartar emetic followed immediately by suramin. A month after the end of treatment, one of them had a blood-poison relapse. She was then treated for 6 weeks with combined neostibosan and suramin followed by pentamidine. The second patient received

a final 3-week course of combined tryparsamide and tartar emetic Both patients appeared quite well 3 months and 5 months, respectively, after discharge from hospital, but are, of course, to be kept under further observation

E M Lourie

TRINQUIER, E & ARNOULT, H Premiers résultats obtenus avec la pentamidine dans le traitement de la maladie du sommeil en A E F [Pentamidine Treatment of Sleeping Sickness in French Equatorial Africa] *Bull Soc Path Exot* 1947, v 40, Nos 9/10, 388-400

The first cases of *T gambiense* sleeping sickness to receive pentamidine in French Equatorial Africa were treated in November 1945

Experience with this compound has confirmed that of other workers It is described as one of the best peripheral sterilizing agents known Early cases can be cured in 10, or perhaps even 5, days It has given excellent results in the treatment of relapses, or of cases refractory to other compounds In the late stages, however, it is inadequate, but combined with tryparsamide it gives results at least as good as those given by any other tryparsamide combination

E M Lourie

SCHUELER, F W The Mechanism of Drug Resistance in Trypanosomes II A Method for the Differential Staining of Normal and Drug Resistant Trypanosomes and its possible relation to the Mechanism of Drug Resistance *J Infect Dis* 1947, Sept-Oct, v 81, No 2, 139-46, 2 figs [30 refs]

The author has compared the staining reactions of normal and of drug-resistant strains of trypanosomes at different hydrogen-ion concentrations

The trypanosome strains were (1) Normal *T equiperdum*, (2) *T equiperdum* resistant to mapharside and *p*-arsenosphenylbutyric acid, (3) Normal *T hippicum*, and (4) *T hippicum* resistant to pentavalent arsenicals

Two purely basic dyes were used, namely, methylene blue (Gruebler) and toluidine blue O (Conn) In some cases the trypanosomes were first treated with arsenicals, in order to study the effect of this on subsequent staining A purely acid dye, bluish eosin (Gruebler) was also used

The findings were interpreted as indicating that the acquirement of drug-resistance involves a significant shift in the isoelectric points of the trypanosome's proteins, particularly in certain localized portions of the trypanosome cell

E M Lourie

CULWICK, A T & FAIRBAIRN, H Polymorphism in *Trypanosoma simiae* and the Morphology of the Metacyclic Forms *Trans Roy Soc Trop Med & Hyg* 1947, Dec, v 41, No 3, 415-18, 1 fig

The authors describe the results of a biometrical study of the morphology of *Trypanosoma simiae*, the causative organism of acute porcine trypanosomiasis The strain which was used for this work was originally isolated from the blood of a horse in Tanganyika, then passaged through two sheep into tsetse-flies (*Glossina morsitans*), from which the trypanosomes were transmitted cyclically in *Cercopithecus* monkeys This study is based on the examination of blood films taken daily from these animals in the course of the infection, which lasted 4-6 days Attempts to infect goats with this strain failed

A statistical analysis of the measurements of this strain confirmed the reviewer's description of *T simiae* [this *Bulletin*, 1936, v 33, 647, 1937, v 34, 524] and showed that the species was trimorphic, comprising (a) long stout forms (*simiae* s s), which were predominant, (b) *rodhaini*-like forms, and (c)

congolense-like forms. Since the long stout forms were the only ones dividing by binary fission, they are regarded as heterozygous, while the other two are said to be homozygous according to the authors' views regarding syngamy in this trypanosome [the *Bulletin* 1947 v 44 649]

Metacyclic trypanosomes (which are depicted) were obtained on slides probed on by infected flies. They are represented by forms with and without a free flagellum measuring 10-12  $\mu$  in length. *T. smias* was also discovered in the blood of cattle. It is thus present under natural conditions not only in its usual host, the pig but also in two new hosts—horse and cattle. In view of the superficial resemblance of some forms of *T. smias* to *T. brucei* and of others to *T. congolense* equine and bovine infections with the first-named species are liable to be misinterpreted, unless the morphology of the trypanosomes present is carefully determined.

C A Hoare

POMER A. de A. with the collaboration of J. L. DE OLIVEIRA & others. A doença de Chagas na Bahia. [Chagas's Disease in Bahia.] *Arquivos Universidade Federal de Med.* 1946 v 1 333-458, 107 figs. on pls. & 2 folding maps. [Refs. in footnotes.] Comments in English.

This monograph is a record of careful work carried out with close attention to detail. Cardiac disease is common in Bahia and the author who is a Professor of Clinical Medicine, has with the assistance of several colleagues, examined patients passing through the Cardiology Department of the Santa Isabel Hospital. His method of procedure was to examine those presenting suspicious symptoms oedema, cyanosis, dyspnoea, palpitation, cardiac enlargement, pleural effusion, ascites, hepatomegaly cardiac murmurs, precordial pain etc., by X-ray by venodiagnostics, and by complement fixation, using Davis's antigen. Ten species of *Triatomas* are found in Bahia, but *P. megistus* seems to be the only important vector. Of 400 nymphs and adults 99 (24.4 per cent.) were found infected with *T. cruzi*. For the xenodiagnostic test 5-8 nymphs and adults were allowed to feed on the patients for on an average 30 minutes. Thereafter they were allowed to feed on chickens and guinea-pigs and were examined 30-60 days after the infecting feed.

Details are given of 37 cases with a number of cardiographic tracings of each, most of them well reproduced. In 11 out of 33 in which the xenodiagnostic methods were carried out the results were positive, a figure closely approximating that of ROMANA and CORREIA who found 34.6 per cent. whereas DIAS recorded only 14.15 per cent. The complement fixation test however gave a positive result in all 33 cases in which it was performed. In the other four xenodiagnosis was positive and the c.f. test was omitted.

The ages of the patients recorded ranged between 8 and 48 years, the majority being in the third and fourth decades and almost half (17 out of 36 whose ages were known) were between 1 and 30 years. The electro-cardiographic changes varied, the commonest being primary changes of the S-T and T waves and A.V. block.

There is a line map indicating the places whence patients came and where infected *P. megistus* were found and there are the usual photographs of children showing Romana's sign.

H. Harold Scott

ROMANA, C. & ABALOS, J. *Triatoma dalponesi* n. sp. (Hemiptera Reduviidae) [*Triatoma dalponesi* n. sp.] *An. Inst. Med. Regional Tucuman Argentina*. 1947 Nov. No. 1 79-93 7 figs. & 2 coloured pls. [14 refs.]

The English summary appended to the paper is as follows —

The authors describe *Triatoma dalponesi* n. sp. collected naturally by *Schizotrypanum cruzi*. Their differential study is made with *Triatoma platensis*

Neiva 1913 *T. delponte* has been obtained exclusively in nests of *Miyopsitta monacha colorra*"

DE FREITAS, J. L. P. Contribuição para o estudo do diagnóstico da moléstia de Chagas por processos de laboratório [Laboratory Methods of Diagnosis of Chagas's Disease] [Thesis for Doctor's Degree] Universidade de São Paulo, Faculdade de Medicina -1947, 160 pp., 2 figs on 1 pl. [Bibliography] English summary

[This thesis is better than the usual run of theses for doctorate in Brazil Universities with which we have become acquainted. It differs much from the usual compilation from the literature for, though references to and quotations from published books and papers are copious, this thesis details a record of a considerable amount of work carefully performed by the author, though, naturally, it is repetitive rather than original.]

The various methods of diagnosing Chagas's disease are taken up in turn, the author has tried them himself in a fairly large number of cases and here puts his findings on record. First, *xenodiagnosis*. This was tested in 550 persons, and 93 (16.9 per cent) proved positive, of 1,025 Triatomidae which fed on patients suffering from Chagas's disease only 212 (20.6 per cent) were infected—not a satisfactory result—and one patient was tested no less than 14 times. Of 32 patients specially mentioned as undergoing the test three times, in 17 it was positive on the first occasion, in 9 on the second, and on the third in the remaining six. Second, *animal inoculation*, with the use of guinea-pigs and rats (camundongos). None of the former (8 only were inoculated) and only 4 of 238 of the latter, inoculated with blood from 38 patients, were infected. Third, *haemoculture* on blood agar was carried out from 21 patients, of whom 12 had given a positive xenodiagnostic test and the other 9 a positive complement fixation. At first, 0.2 cc of blood was inoculated but without result, so 0.5 cc was tried, but again all were negative. Fourth, *complement fixation*. The author divided the cases so tested into groups: (1) Those definitely infected with the trypanosome as evidenced by positive xenodiagnosis, by animal inoculation, or the finding of leishmania forms in the myocardium at autopsy. Of 75 in this group a strongly positive result was obtained in 71 and in two others it was weakly positive giving 97.3 per cent positive. (2) Those with lesions present or healed, of muco-cutaneous leishmaniasis. There were 44 of these and in all cases where the result was positive Chagas's disease was proved to be present also, or was strongly suspected. Where there was no such suspicion the result was negative, as it was also in group 3, syphilitic patients or those suffering from other diseases than Chagas's disease, such as malaria, soft chancre, blastomycosis, lymphogranuloma inguinale, glandular tuberculosis, and infectious mononucleosis. It is true that two patients with chancroid gave a positive c f test, but one definitely had Chagas's disease and the other lived in a district heavily infested with Triatomidae. In two among 34 with leprosy, in whom Chagas's disease could be excluded, the c f test was nevertheless positive. This test, even when the blood gave a strong positive, proved negative with the spinal fluid.

Other serological tests mentioned are the agglutination reaction, precipitation reactions with culture extracts, and the intradermal reaction with heart extract as reagent, which was negative in all cases tried.

The author concludes: "Xenodiagnosis is the best method to show the presence of *T. cruzi* in the blood of chronic cases of Chagas's disease. However, as in a large number of patients this test may be negative, the complement fixation test, employing *T. cruzi* antigen, is deemed the most valuable process for the diagnosis of the disease." [A praiseworthy and well documented piece of work.]

H. Harold Scott

- ROMANA, C. & GI, J. Xenodiagnostico artificial. [Artificial Xenodiagnosis.] *An. Inst. Med. Regional Tucuman, Argentina.* 1947 Nov v 2, No. 1 57-60 1 fig.

The English summary appended to the paper is as follows —

The authors describe a dispositive for practising artificial xenodiagnosis for cases in which it is not possible to perform it directly upon the patients. It consists of a tube closed with the skin of a laboratory animal which contains the suspected defibrinated or citrated blood. The triatomid bugs are placed in another tube in which is inserted the first mentioned. By this method they have obtained positive human xenodiagnosis."

- BARRETO, A. L. de B. Provas subcláticas no diagnóstico da doença de Chagas. [Subclavian Tests in the Diagnosis of Chagas's Disease.] *Arquivos Univ. Bahia Facul. de Med.* 1948, v 1 285-320 [78 refs.] English summary

- ROMANA, C. Miocarditis crónica esquistotripanosica. (Hallazgo de *Schizotrypanum cruzi* en el corazón) [Chronic Myocarditis in Infection with *Trypanosoma cruzi*.] *An. Inst. Med. Regional, Tucuman, Argentina.* 1947 Nov v 2, No. 1 1-18 15 text figs. & 2 coloured figs. on 1 pl.

The English summary appended to the paper is as follows —

"The clinical history is related of a patient with a supposed diagnosis of cardiac form of Chagas disease. In the autopsy there were found in the heart lesions of chronic infiltrative and sclerotic myocarditis and dividing forms of *S. cruzi*. In the epicardium and especially in the fibrous auriculo-ventricular circular band were observed great cellular accumulations in which the lymphoid cells predominate the true character of which is discussed in the text."

- ROMANA, C. Encefalopatías de posible origen esquistotripanosico. [Encephalopathy possibly caused by *Trypanosoma cruzi* Infection.] *An. Inst. Med. Regional Tucuman, Argentina.* 1947 Nov v 2, No. 1 19-30 5 figs.

The English summary appended to the paper is as follows —

"The author after commenting on the present state of knowledge of the nervous forms of the Chagas disease relates the clinical history of three cases of chronic encephalopathy in which the only possible cause manifested was the *S. cruzi* infection."

"The patients present a syndrome of psychic states and of spastic paralysis which agree with the classical descriptions which Chagas and Viñela gave for the nervous forms of the disease."

## LEISHMANIASIS

- BALLABRIGA A. A propos des manifestations cliniques et des complications du kala azar infantile. [Infantile Kala-Azar] *A n. Pediatrics* 1948, Dec. v 167 No. 6 364-72 5 figs.

The paper gives an account of 40 cases of infantile kala azar which the author had under her care in Barcelona during the past three years. The symptoms described are typical of the disease which is said to be quite common in Spain.

C. M. WYSON

Row, R & PATKAR, N A Kala-Azar of Undoubted Indigenous Origin discovered in Dry Areas *Indian Physician* 1947 Nov, v 6, No 11, 251-3

Report of a case from Bombay

MOST, H & LAVIETES, P 'H Kala Azar in American Military Personnel Report of 30 Cases *Medicine* 1947, Sept, v 26, No 3, 221-84, 10 figs [24 refs]

During, or as a result of, World War II, 50 to 75 cases of kala azar occurred in members of the United States Army. Most of these cases were studied very carefully and thirty came within the direct experience of the authors. These thirty cases form the basis of this paper, which is an excellent study of kala azar, primarily clinical in outlook. It will naturally be impossible to do it justice in a short summary.

Fifteen patients acquired the infection in India and 15 in the Mediterranean area, North Africa, Sicily or Italy, in the latter group was included a man who had served in London, Paris and Nice, the last for only one week three weeks before the onset of symptoms.

Most of the patients had spent nights in native villages within the endemic areas. Two officers lived in the same billet in Calcutta. [The reviewer was consulted by one of them in the U S A, and ascertained that these two officers shared a ground-floor flat in a part of Calcutta which he knew well as a highly endemic area.] The incubation period varied from 3 weeks in one case, to at least 19 months in another.

The onset was sudden, with fever, in 29 cases. The fever showed a double rise during the day in fifteen cases. One patient was afebrile throughout the observed course of the disease. Headache occurred in eight persons and was the commonest of the minor symptoms. Loss of weight was almost constant, but despite this and the fever, few of the patients appeared to be acutely ill at any stage of the disease. The tongue was not usually coated. In seven patients, cervical adenopathy was prominent, in 5, gland biopsy showed leishmania either at the first examination or on re-examination of the sections. No heart changes were noted.

The spleen was found enlarged in 27 patients at first examination, and in the other three enlargement developed later, 22 had enlarged livers at some stage of the disease. The spleen varied in size from being just palpable to reaching well below the umbilicus, the enlargement was very rapid, in some cases this level was reached within three months. There were no mental or neurological changes.

In almost every case malaria was suspected at first. The other febrile diseases considered were brucellosis in five cases, subacute bacterial endocarditis and military tuberculosis each in one case, dengue in two, typhoid or typhus in five, amoebiasis in three, pneumonia in two patients, one of whom actually had pneumonia also, infective hepatitis in two, histoplasmosis in one, nephritis in two and in nine cases, fever of uncertain origin (FUO) was the last diagnosis when the patients were transferred to a general hospital "after continued study and failure to establish a diagnosis." In addition to these, "Hodgkin's disease, acute aleukaemic leukaemia, aplastic anaemia and infectious mononucleosis were considered seriously in approximately 50 per cent of our cases, and in some patients one of these diagnoses was considered tenable for at least three months."

Sternal puncture was performed on 29 patients on one or more occasions, the first puncture was positive in 14, subsequent punctures in seven, and a negative puncture only was recorded in eight cases. Spleen puncture was performed on 18 patients and gave positive results in all.

The average period from onset of symptoms to diagnosis was 10 weeks and six patients were under observation in hospital from 4 to 8 months before a diagnosis of kala azar was made.

The drugs used were foudadin, neostam, stibanose, neostibosan and stilbamidine and the percentage case cure rates were 0, 42, 50, 93 and 100. foudadin and stilbamidine were used only in two cases each.

Neostibosan was given in total doses of 50 grammes in 10 to 17 days intravenously in a 5 per cent. solution. No toxic symptoms were observed. Toxic symptoms were observed in most of the patients who received neostam. The failures with neostibosan were usually due to inadequate dosage; one patient however after having had small amounts of foudadin, neostam and neostibosan overseas received two courses of neostibosan, of 5 and 10 grammes respectively and one of stibanose without permanent improvement; he was eventually cured by 4.0 grammes of stilbamidine.

"Naper's formol-gel test" was positive in only half the cases in the first three months, but in 12 out of 14 after three months. The correlation with hyperglobulinæmia was not complete as occasionally, especially after treatment a clear firm gel (negative) occurred in the presence of over 4% per cent. of globulin. Electrophoretic studies were made and it was concluded that the globulin peculiar to leishmaniasis is a soluble gamma globulin which binds subnormal amounts of calcium. The authors suggest that it arises as an immune reaction or as a result of destruction of parasitized reticulo-endothelial cells.

Leucopenia and granulopenia were constant findings. 15 out of 23 patients had white counts below 4,000 per cmm. at the first examination and three out of 11 who were examined within the first 10 days of symptoms had counts below this figure. A count below 1,000 white cells or 500 granulocytes were encountered.

The red cell counts in 20 cases observed before treatment in the Moore General Hospital were all between 2.91 and 3.86 millions and within one month of successful treatment they ranged between 3.51 and 4.50 millions. The cells were usually slightly hypochromic and slightly macrocytic.

There was no marked prolongation of bleeding time or clotting time, but in a few cases clot retraction was retarded. The platelet counts were all subnormal, but extreme degrees of thrombocytopenia were not observed. Serum calcium was in the lower normal range.

The reticulocyte count was normally low before treatment and the authors claim that a significant crisis occurred in each of the six cases followed through treatment; the peak, which was over 10 per cent. in only two cases, namely 14.8 per cent. and 15 per cent. occurred between the 13th and 18th days after the first injection.

The erythrocyte sedimentation rate was usually but not constantly increased; it was not found of any value in predicting the activity of the disease.

There was no indication of liver dysfunction before, during or after treatment.

Out of 25 patients observed during an acute period of the disease 16 showed albumin in the urine, 12 macroscopic hæmaturia, and in two there were clinically important renal complications. There was one case of chronic renal insufficiency after successful treatment with neostibosan and in another a classical acute glomerulo-nephritis developed; this was approximately coincident with the onset of kala azar.

The paper includes individual case reports of these 30 cases.

The 24 references are 11 papers and books published in the United States or China; the vast literature that has emanated from Europe, North Africa, and India is ignored. [The reviewer's predominating impression on reading this important paper is that it demonstrates what an extraordinarily standardized





The question of the removal of the spleen has to be considered under four headings—namely its effect on the leishmaniasis, the anaemia, the leucopenia and the comfort of the patient. It was thought that the infection was possibly persisting in the spleen where it could not be reached in sufficient concentration by the anti-leishmania drugs. The persistent anaemia despite many blood transfusions might be produced by the enlarged spleen in several different ways—by providing a large haemostatic pool for blood and thereby increasing haemolysis—by providing an increase of reticulo-endothelial tissue which itself might increase blood destruction directly or indirectly by increasing the globulin in the blood and causing pseudo-agglutination and rouleau formation—or by splenic control of haemopoiesis. Hypersplenic conditions are also recognized as a cause of granulopenia. In this case the operation was successful on all four counts.

References in the literature to splenectomy in kala azar are discussed. These included two successful cases reported by MARTIN CHORINE and ROUSSET (*this Bulletin* 1938, v 33 30) and SWERKEY, FRIEDLANDER and QUINN (*ibid.* 1946 v 43 114).

L. E. A. JAR

COLLARD P. J. & HARGREAVES W. H. Neuropathy after Stilbamidine Treatment of Kala-Azar. *Lancet* 1947 Nov 8 686-8. [11 refs.]

A peculiar nervous sequel to the treatment of kala azar by stilbamidine was pointed out by NAPIER and SEN GUPTA (*this Bulletin* 1942 v 39 748). This consisted of paraesthesia and anaesthesia of the face in the distribution of the trigeminal nerve. Later SEN GUPTA (*ibid.* 1944 v 41 273) reported it as occurring in 17 of 101 patients given the drug.

QASTLER and FIDLER (*ibid.* 1946 v 43 1029) reported that two patients treated for Sudanese kala azar by stilbamidine had died, late in convalescence from enal hepatic and pancreatic damage. Similar lesions were produced in dogs by the same solution, but no lesions were produced by a freshly prepared solution. However YORKE and FULTON (*ibid.* 1948 v 40 23) and FULTON (*ibid.* 683) showed that although the freshly prepared solution did not produce lesions in these organs, it did produce lesions in the central nervous system.

The present authors' first patient was invalided from Malta in November 1943 with kala azar—he failed to respond to two courses of neostam but did so dramatically to a course consisting of 1.45 gm. of stilbamidine. A steady flow of cases of kala azar came in from North Africa, Sicily and Italy and stilbamidine was given in most cases with excellent immediate results—but by the end of 1944 an alarming number of cases with facial symptoms had been found during the follow up and subsequently this drug was replaced by carbostilamide and urea stilbamidine.

Of 4 cases in which stilbamidine was used, 22 developed the neuropathy 2 to 8 months after completion of treatment—the other two patients were not seen, but made no complaint of these lesions in their answers to a written questionnaire.

The symptoms were anaesthesia of the face and sometimes of the neck, scalp and chest; paraesthesia; hyperaesthesia so that light touch or shaving caused an agonizing pain; itching of the eyelids; watering of the eyes and blinking. The skin over the same area was sometimes dry and atrophic. The corneal reflex was depressed but never lost. The condition remained at its maximum up to 18 months and then gradually improved. No treatment had any effect. The disability was a serious one.

Napier and Sen Gupta (*loc. cit.*) suggested that the lesion was in the principal sensory nucleus of the trigeminal nerve and that it might extend caudally in the spinal tract. The authors consider that the lesion may extend further into the

central grey matter near the substantia gelatinosa Rolandi. The drug is related by its ethylene linkage to trichlorethylene, which also affects the cranial nerve nuclei, especially the fifth

L E Napier

MANGABEIRA-ALBERNAZ, P. Estudo critico do "pólipo da leishmaniose" [Critical Study of the "Leishmanial Polyp"] *Brasil-Médico* 1947, Aug 2 & 9, 16, 23 & 30, Sept 6 & 13, v 61, Nos 31-32, 33-34-35, 36-37, pp 283-91, 301-6, 319-23, 19 figs [70 refs]

The author more than 20 years ago described polyp of the nasal septum in leishmaniasis (*Ciência Médica*, 1925, v 3, 113 and *Arch Internat de Laryngol* 1926, v 32, 139) and under the title "the Leishmania polyp" in *Brasil-Médico*, 1928, v 42, 729) [In spite of this it is not mentioned in textbooks of Tropical Medicine, though STIRR has a brief reference to oro-nasal leishmaniasis in his chapter dealing with leprosy]

In the present article, the author describes in detail and depicts in photographs and drawings four forms of the condition (1) The fibrous sessile type, (2) The peduncular mucoid type (3) The pendulous, the most common in which the tumour moves in the perforated septum, and (4) The diffuse hyperplastic. The histology is shown in a series of photomicrographs and the distinctions between this and tuberculous, syphilitic and other nasal tumours. On the scar or base of a leishmanial lesion a non-leishmanial tumour may grow. One illustration shows an angiofibroma which was removed from the nose and which had been growing from the edge of a leishmanial perforation of the septum. Twenty-eight cases are recorded in this paper

H Harold Scott

## FEVERS OF THE TYPHUS GROUP

SMADL, J E, JACKSON, Elizabeth B & GAULD, R L. Factors influencing the Growth of Rickettsiae. I. Rickettsiostatic Effect of Streptomycin in Experimental Infections. *J Immunology* 1947, Nov v 57, No 3, 273-81, 1 fig [11 refs]

This study is in continuation of the investigation referred to in this *Bulletin*, 1948, v 45, 168

Strains of *Rickettsia prowazekii*, *R mooseri*, *R orientalis*, *R akari*, and *Dermacentorinus* [*Rickettsia*] *rickettsi* were cultivated in yolk sacs and employed in the tests in the usual way

Doses of 10-20 mgm of streptomycin produced an appreciable inhibitory effect on all the rickettsiae except *R orientalis*, *R akari* was most strongly affected. The addition of 0.4 mgm of nitroacridin to 10 mgm doses of streptomycin caused an additional degree of inhibition of growth of *R mooseri*, and *R rickettsi*, but not of *R akari*. The addition of 0.5 mgm of para-aminobenzoic acid caused a pronounced degree of additional inhibition of growth of all the organisms except *R orientalis*. These synergic effects are regarded as being of possible importance in connexion with treatment of the diseases

John W D Megaw

CAMAIN R. Sur une similitude d'affinités tinctoriales. Limitation des résultats donnés par la coloration des rickettsiales au Machiavello et au Giemsa bouillant. [Limitations in the Results obtained by Staining of Rickettsiae by Machiavello's Method and Hot Giemsa.] *Bull. Soc. Path. Exot* 1947 v 40 Nov. 9/10 325-6.

The author examined the possibility of finding in certain micro-organisms inclusions having staining properties analogous to those of the ruby-red homogeneous bodies found in typhus material by GIBSON and PARMER (*this Bulletin*, 1942, v 39 733).

He used the routine stain employed in his laboratory namely boiling Giemsa and Machiavello to stain blood films from mice infected with *Trypanosoma gambiense*. In this way, he was able to demonstrate grains of volutin in the anterior part of the cytoplasm. Nevertheless, the author believes that the supposed affinity in staining properties between volutin and rickettsial bodies is only apparent because when the different processes in Machiavello's method are tested and analysed separately it will be seen that if the methylene blue counterstain alone is used, the rickettsiae stain pale blue but the volutin now stains violet black yet with combinations of fuchsin citric acid and methylene blue used in the full staining process, rickettsiae and volutin alike stain reddish purple. Since it is also known that the rickettsiae of scrub typhus take only the blue stain by Machiavello's method, the author concludes that, whatever the nature of volutin and of the inclusions in higher organisms tinctorially resembling it the use of Machiavello's method and of hot Giemsa do not provide a certain diagnostic criterion for detecting rickettsiae.

H J O D Burke-Gaffney

BISAGNI G. Tifo esantematico benigno a Cagliari. [Mild Epidemic Typhus in Cagliari.] *Atta Med. Italia* 1947 Oct. v 2, No. 10 327-R. English summary (3 lines)

An account of 24 cases.

MONTGOMERY T H L & BUDDEN F H Typhus in Northern Nigeria. I. Epidemiological Studies. *Trans. Roy. Soc. Trop. Med. & Hyg.* 1947 Dec. v 41 No. 3 327-37 2 figs. & 2 graphs.

An outbreak of louse-borne typhus occurred during the months June to September 1945 in Jos, a town of about 20 000 inhabitants situated at a height of about 4 000 feet on the Bauchi Plateau North Nigeria. The cases detected numbered 128 of these 32 were fatal.

All the attacks occurred among persons living in 58 of the 1,600 compounds contained in the town. Louse infestation was heavy and almost universal.

In 92 cases, Weil-Felix titre of more than 1/100 was observed.

Despite early difficulties dusting with DDT powder soon became effective and when the people experienced the comfort of being free from lice and bedbugs they clamoured for the powder.

The authors stated that spare clothing, etc. after being dusted, were kept for 48 hours in closed dustbins no lice survived this treatment.

John W D Megey

FINDLAY G M & ELMES B G T Typhus in Northern Nigeria. II. Laboratory Investigations. *Trans. Roy. Soc. Trop. Med. & Hyg.* 1947 Dec. 41 No. 3 339-52. (14 refs.)

The authors describe their very thorough laboratory investigation into the outbreak of typhus fever referred to in the previous abstract.

Rickettsiae were isolated by guineapig inoculation from five out of seven batches (30-40 in each) of lice collected from patients, and from the blood of nine out of ten patients. Some of the human strains were passaged 7 to 20 times serially through guineapigs. In the early passages all the strains caused some degree of scrotal reaction, but after the 8th to 10th passages few reactions occurred, and none was observed after the 15th passage. Mooser cells were very occasionally seen in the tunica exudate. Rickettsiae were isolated from fleas (*Xenopsylla cheopis*) that had been caused to feed on a giant bush rat (*Cricetomys gambianus*) previously inoculated with one of the strains, but this observation was not regarded as showing that the strain was murine.

The sera of 92 patients gave high-titre agglutinations with *Proteus* strains—82 with OX19 and 10 with OX2. Of 31 sera tested for rickettsia agglutination, 27 gave higher-titre reactions with epidemic than with murine strains, the remaining four reacted more strongly with murine strains. Four sera were tested by the complement-fixation test, two reacted more strongly with epidemic than with murine antigens and two reacted at the same high titres with both antigens.

Various animals were tested for susceptibility to inoculation with suspensions of brains and spleens of infected guineapigs, the intraperitoneal route was employed except when otherwise stated.

In rabbits, a thermal reaction was sometimes produced, and in other rabbits inoculated intratracheally, fever and patchy pneumonia developed, rickettsiae were found in lung smears. Dogs showed no obvious reaction, but their blood on the 8th to the 15th day was infective to guineapigs. Out of seven green monkeys (*Cercopithecus aethiops centralis*) three gave a febrile response and their blood was infective to guineapigs. Another green monkey was inoculated intratracheally, a febrile reaction followed and rickettsiae were found in the lungs and blood. Eight other monkeys, belonging to four different species, were inoculated, there were no apparent reactions but the blood of two became infective to guineapigs. White mice were not affected by intranasal inoculation of the suspensions, but developed patchy pneumonia when suspensions of infected rabbits' lungs were used, and five successive lung passages were made.

Several kinds of wild rodents gave no apparent reactions, but infection was found in their blood.

The authors mention that flea-borne typhus is known to be widely distributed in West Africa and they refer to unpublished observations which strongly suggest that tick-borne infection also occurs. They state that rickettsiae were isolated from the blood of a European officer in Bauchi, Nigeria, and that his serum gave a positive complement-fixation reaction with a South African tick typhus antigen, but not with murine or epidemic antigens. The serum gave a negative rickettsia-agglutination reaction with epidemic and murine rickettsiae. Two similar cases are said to have occurred in North Ashanti.

A very puzzling case is described as occurring at Kaduna, 180 miles distant from Jos. Just before admission to hospital the patient found, attached to her scalp, a flat, oval, six-legged, "insect", about one-eighth of an inch long, brown in colour with diffuse mottling. At the site of attachment there was afterwards an eschar with local adenitis.

The rash was maculo-papular, it involved the palms and soles. On the 17th day the OX2 titre was 1-320 and the OX19 titre only 1-20.

The complement-fixation titre was found by Major J. Gear, S. A. A. M. C. to be 1-50 with each of four strains of epidemic antigen and 1-12.5 with murine and tick-borne antigens. Rickettsia agglutination was at 1-100 with epidemic and at 1-25 with murine strains.

Rickettsiae were isolated from the patient's blood in the earlier passages through guinea-pigs there was a pronounced haemorrhagic scrotal reaction, but this did not occur in the later passages. Cross immunity with the Jos strain was shown by guinea-pig inoculation.

No known case of rickettsial infection could be discovered from which the patient might have been infected.

The authors state that the history of an insect bite and the occurrence of an eschar suggested tick-borne infection and the behaviour of the strain in guinea-pigs suggested murine infection but the serological reactions were weighty evidence for an epidemic strain.

This is distinctly a problem case. Other points in favour of a tick-borne infection are the type and distribution of the rash, the OX19 type of Weil-Felix reaction, and the absence of any evidence of other source of infection. Either of the two sets of conflicting evidence might be regarded as conclusive, but one must be wrong.

John W D Megees

MONTGOMERY T. H. L. & BUDDEX, F. H. Typhus in Northern Nigeria. III. Clinical Studies. *Trans. Roy. Soc. Trop. Med. & Hyg.* 1947 Dec., v. 41 No. 3 353-62, 3 charts.

This paper contains a description of the clinical features of the outbreak referred to in the previous two papers. The authors state that the clinical picture did not conform to the classical text-book descriptions of louse-borne typhus in the following respects —there was complete absence of rash, diarrhoea, vomiting, gangrene, pressure sores, venous thrombosis, and pupillary contraction. (But the absence of a rash is quite usual among dark-skinned persons and the other features mentioned above are often missing in outbreaks of the disease.)

John W D Megees

GORTIA, R. S. Contribución al estudio de la sedimentación globular en enfermos de tifo exantemático. (A Contribution to the Study of the Erythrocyte-Sedimentation Rate in Typhus Patients.) *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico, 1947 June v. 8, No. 7 97-117 11 charts. English summary.

The author describes the results of a systematic study of the changes occurring in the sedimentation rate at different stages of attacks of typhus fever. Of the 78 patients tested, 61 had classical, and 17 had murine typhus.

In most of the cases there was a progressive increase in the sedimentation rate till the end of the first week of convalescence, and then a very slow return towards normal, but many irregularities were observed. In mild attacks there was little or no departure from the normal. Complications gave rise to sudden increase in the rate. Among six fatal cases in which there were no complications, three showed no sedimentation, one showed a normal rate, and in the other two the rate increased progressively till the day of death when a sudden return to normal was observed.

On the whole there was a direct relationship between the degree of increase in the acceleration of the sedimentation rate and the severity of the illness, but there were striking exceptions to this rule.

The method employed was that described by CUTLER (*Amer. J. Med. Sci.* 1932, v. 183 643). Illustrative curves and details of the average rates observed at various stages of the illness are presented.

John W D Megees

RAVENAL, J. H. Relationship between the Incidence of Typhus Fever among the Human and Murine Populations of Shanghai. *Chinese Med J Shanghai* 1947, July-Aug., v 65, Nos. 7 & 211-24. [15 refs.]

Two papers by the same author dealing at greater length with the same subject have already been reviewed (this *Bulletin* 1947, v 14, 893, 1059).

IN W. T. CHANG, I. L. & LIN C. C. Typhus Fever in Chengtu. A Clinical Study of 184 Cases. *Chinese Med J Shanghai* 1947, July-Aug. v 65, Nos. 7 & 199-210. 23 refs.

The authors saw 184 cases of typhus fever in two hospitals in Chengtu during the years 1940-1944. The great majority of the cases appear to have been flea-borne. The incidence month by month was as follows: January, 10; February, 9; March, 9; April, 14; May, 7; June, 5; July, 9; August, 16; September, 37; October, 27; November, 27; and December, 14. There was no evidence of transmission to contacts except perhaps in a few acute cases occurring during the winter and the spring among persons who had recently arrived in Chengtu after travelling from distant places.

Among the Weil-Felix tests that were carried out 75 patients gave positive reactions with *Proteus OX19*; of these 59 also reacted with *OX2* and 7 with *OXA*. Three patients who gave negative reactions with *OX19* reacted with *OX2* at a titre of 1-160. *John W. D. Megaw.*

NYKA, W. Development of the Inflammatory Lesions and of Rickettsiae of Murine Typhus in the Lungs of Rats. *Israel J Pathol.* 1947, Sept. v 23, No. 5, 843-56. 42 figs. on 3 pls.

The histological changes observed in the lungs of rats sacrificed at intervals ranging from three minutes to 72 hours after inoculation by the nasal route with suspensions of murine rickettsiae are described.

The main part of the paper consists of a description of the development of the rickettsiae in the same lungs.

As early as five hours after inoculation, adult rods and diplococci are found, some of them in small intracellular clumps which are regarded as the earliest forms of rickettsial colonies developing from "dot forms" of the organisms. Later the clumps enlarge and rods and diplococci are seen to emerge from them and often to escape from the cells and enter other cells in which they continue to multiply.

After about 48 hours, pronounced extracellular multiplication is observed, associated with the formation of clumps which here as well as inside the cells sometimes grow to a considerable size. No evidence was found to support the view that invisible forms of the organism occur and the clumps are regarded as being nothing more than colonies of rickettsiae; there seemed to be no reason to assume that they represent a special developmental phase in the life cycle of the organisms.

The description of the multiplication of the rickettsiae is attractively simple, every statement is supported by a reference to one or more of the 32 clear photomicrographs which illustrate the paper. *John W. D. Megaw.*

JADIN, J. Fièvre rouge congolaise ou typhus murin à Costermansville. [The Red Fever of the Congo or Murine Typhus at Costermansville]. *Ann Soc Belge de Méd Trop.* 1947, June 30, v 27, No. 2, 231-40, 1 chart. [18 refs.]

Orchitic strains of rickettsiae, regarded as of murine type, were isolated from two out of five patients who were regarded as suffering from "fièvre rouge".







## PLAGUE

HENRY E. B. Laboratory Studies on the Biogenetics of the Rat Fleas, *Xenopsylla brasiliensis* Baker and *Y. cheopis* Roths. III. Further Factors affecting Adult Longevity *Bull. Entom. Res.* 1947 Dec. v 38 Pt. 3, 399-404 [16 refs.]

The length of life of the adult *Xenopsylla* is of considerable importance in relation to the possible carriage of plague infection in merchandise also because one collection of data appeared to show a simple linear relation between length of life of the starved flea and saturation deficiency of the atmosphere. Since then large and puzzling anomalies have been recorded by HORTON [this Bulletin 1938, v 33 359], LUNSON [ibid. 879] and others. The subject seems to become less comprehensible as more work is done on it.

The present author has cleared up at least some of the anomalies. He shows that if the larvae (*X. brasiliensis* and a few experiments with *cheopis*) are reared together in a culture jar the adults live for a significantly shorter period than if the larvae are reared singly. Moreover old parent fleas lay eggs which give rise to adult progeny which are shorter lived than those of younger parents. Several other factors influencing the length of life of the starved adult flea are identified.

It is found that if the larval food is contaminated by the droppings of the mouse this has no significant effect on the length of life of the adult fleas (an unexpected result for the droppings would be supposed to be a source of B vitamins derived from micro-organisms presumably other material in the breeding medium provides these vitamins). Another unexpected but apparently well-established result is that unfed fleas live longer under several different standard conditions than those which have been fed once and then starved. [For previous papers in this series, see this Bulletin 1945 v 42, 504 1947 v 44 1103.] P. A. BURTON

SIMMONS, A. T. W. & CHAKRABARTY K. D. Further Observations on Plague. *Indian Med. Gaz.* 1947 Aug. v 82, No. 8, 447-51 3 figs.

DDT especially, seems to have been popular with villagers, because incidentally it got rid not only of fleas but also of bedbugs, flies and other pests. Curiously enough, the use of cyanogas and kerosene soap emulsion as an anti epidemic measure, formerly advocated is now regarded as "a too radical destruction of rats" and as having a merely ephemeral effect on fleas, so that on occasion it was followed by a sudden rise in plague incidence. W. T. Hurst,

KARASIMHANDI P. V. & RAO, K. S. Streptomycin in Human Plague. *Lancet* 1948 Jan. 3 22-51gs

In this preliminary communication relating to an epidemic of 152 cases and 66 deaths five moribund plague patients were treated with intramuscular streptomycin only. The dose was 0.125 gm. every 3 hours for 72-96 hours. Improvement was evident with a total of 1.5 gm.; no toxic effects were noted and all patients are now alive and well. Temperature charts and details are given. The five patients appear to have been the only cases treated as the supply of streptomycin became exhausted. W. T. Hurst

ROBERTS, J. M. & GORDON, H. Plague: a Survey of Recent Developments in the Prevention and Treatment of the Disease. *Inter J Trop Med* 1947, Nov. 5 27 No. 6 1932-2016

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## CHOLERA

- i. STRAUSS W. The Cholera Epidemic in Egypt and its Potential Danger to Palestine. *Harefuah*. Jerusalem. 1947 Dec. 1 v 33 No. 11 [In Hebrew 173-4 1 map. English summary 174]
- ii. SILBERSTEIN W. Preventive Inoculation against Cholera. *Ibid.* [In Hebrew 174-5. English summary 175.]
- iii. STEINITZ E. Notes on a Cholera Epidemic in Burma. *Ibid.* [In Hebrew 175-7. English summary 177.]

i. Measures taken by the Palestine authorities to limit the penetration of isolated cases of cholera from Egypt make the danger of the epidemic spreading to Palestine comparatively small. The author considers that the danger will increase at the end of the Egyptian epidemic when carriers may pass over the re-opened frontier. This eventuality must be met with the strictest measures to protect drinking water and food and the supervision of sanitation generally. It is considered that mass vaccination throughout Palestine would be premature, especially because of its uncertain and short-lived effects.

ii. The author discusses the theory and history of inoculation against cholera and points out that it is not analogous to anti-typhoid inoculation since the cholera vibrio is not brought into direct contact with the blood serum.

In Palestine at present the inoculation consists of two weekly injections (0.5 and 1.0 cc.) of a heat-killed vaccine containing 2 000 million organisms per cc. Reactions are sometimes severe. Pain and oedema where they occur usually last for 48 hours and general reactions are quite frequently severe comprising fever, nausea and vomiting, up to 72 hours. In about 10 per cent. of cases, there is transitory diarrhoea on the second day. It is made clear that preventive inoculation is only one of many preventive measures.

iii. A small cholera epidemic in Central Burma in August 1945 is described. Infection was traced to the indiscriminate drinking of water by Indian and African troops on the shallow shore of the Irrawaddy. Where dehydration was marked, colossal doses of intra venous saline or glucose saline were given and relapses occurred if this fluid replacement was ceased prematurely. Milder cases were treated with sulphagmankine. The author attributes the low death rate of 4 per cent. to immediate treatment, early inoculation and the probably low virulence of the vibrio. It is emphasized that effective treatment should always be given at the centre of an epidemic and that cholera patients should not be transported for long distances.

H. J. O'D. Burke-Gaffney

SHRIVASTAVA, D. L. & WHITE, P. B. Note on the Relationship of the so-called Ogawa and Inaba Types of *V. cholerae*. *Indian J Med Res.* 1947 July v 35 No. 3 117-29.

[An opinion might be hazarded that some bacteriologists especially those not engaged on definite investigation are none too satisfied with the validity of bacterial species generally. Statistically experience illustrates the powerful influence of selection technical selection the idea of transmutation seems to have something of the grip of a taboo when, to come closer to the subject in hand one found how paracholera vibrios tended to increase in number proportionately to the patience of the worker. One wondered whether failure to produce a greater number might have been reduced by more leisureed and amiable study.] The authors have done great service to the controversy on the true cholera vibrio in declaring (1) their finding of mixtures where dual serological types presented themselves in colonies (2) their belief in the possibility of races presenting trivalent agglutinative properties and (3) as a counter to a bacteriological stigma of complexity in taxonomy—their happier position of urging a simplification of ideas. In short they declare that the

system of subsidiary classification of *V. cholerae* at present in vogue—and in the popularization of which one of us has played some part—is, whatever may subsequently prove to be its practical importance, taxonomically invalid." The article must be read entire for its implications. Some of the summary may be quoted also —

(1) "From 10 strains of *V. cholerae* and 3 strains of *V. El Tor* belonging to the Ogawa type and grown in the presence of Ogawa mono-specific antiserum, there were isolated in each case races serologically indistinguishable from strains of the Inaba type" (2) "When similarly exposed to the action of mono-specific Inaba antiserum, 4 of 8 strains of *V. cholerae*, predominantly Inaba-like in serology, but possessed of an imperfect Ogawa factor, yielded cultures of the Ogawa type" (3) "The existing classification of the vibrios of 'O' group I into serological types is taxonomically invalid."

W F Harvey

BURROWS, W, ELLIOTT, Marian E & HAVENS, Isabelle. Studies on Immunity to Asiatic Cholera. IV. The Excretion of Coproantibody in Experimental Enteric Cholera in the Guinea Pig. *J Infect Dis* 1947, Nov-Dec, v 81, No 3, 261-81, 9 figs [12 refs]

This is a fourth of a series of papers by BURROWS *et al* [this *Bulletin*, 1947, v 44, 422, 1948 v 45, 178]

Provision is finally made by the authors for clear understanding of a difficult argument in a discussion, a summary and a series of conclusions. Distinctions are drawn between intoxication through dosage and real infection, serum- and copro-antibody, local enteric and systemic infection, effective and non-effective immunity, secretion, excretion and leakage of immune body through the intestinal wall and permeability to antigen, apparent diminution in number of faecal vibrios due to agglutination and real diminution due to establishment of copro-immunization, diagnostic, prognostic and prophylactic implications, etc.

The original animal test of Koch by means of young guineapigs and alkalization did not distinguish between toxæmia from overdose of the organisms and true establishment of infection. This has been declared capable of being a true infection by the authors, who show as much even as a 900 per cent multiplication of vibrios within the gut. At first, the strains of vibrio obtained were highly virulent and capable of giving rise to a fatal infection in the guineapigs but later it was no longer possible to produce real fatal infection. A non-fatal infection distinct from fatal toxæmia could, however, be produced and the guinea pig faecal pattern test with its similarity to human cholera infection provides a convenient tool for the study of this disease. The argument must be followed in all its detail. It was found by quantitative studies that — (1) the infection was enteric and this was not invalidated by ability to cultivate vibrios from the spleen though they were found there only in  $\frac{1}{3}$  to  $\frac{1}{2}$  of the animals. (2) non-fatal infection, originally fatal by inoculation of 25 mgm (50 000 million vibrios), could be produced with as little as 7 mgm of vibrios, (3) excretion of vibrios by the infected normal animal showed a characteristic pattern the vibrios making up 40 per cent to 90 per cent of the total faecal flora in the two to four days after infection. (4) alteration of the pattern in animals with a prior non fatal infection, or its equivalent of active parenterally produced immunity showed 'a sharp reduction in numbers excreted early in the infection to 10 per cent to 20 per cent of the total faecal flora and a reduction in time of persistence of infection'. The alteration did not occur in lethal infections where the percentage remained at 90 per cent or higher, (5) agglutination and protective antibody but not bacteriophage could be demonstrated

in faecal fluid obtained by centrifuging and filtering through coarse paper. This antibody was called coproantibody and seems to have been identical with serum antibody although the mechanism by which it appears in the bowel and "contributes to immunity to enteric infection is not apparent from the reported experiments (6) the coproantibody appeared early even before the peak of serum antibody and disappeared in 3 to 4 weeks although serum antibody persisted (7) an immunity-faecal pattern was presented when vibrio excretion was associated with the presence of coproantibody at the time of infection and the reduction of vibrio numbers was real. *W F Harvey*

MONTHLY BULL. MINISTRY OF HEALTH & PUB. HEALTH LAB. SERVICE  
(DIRECTED BY MED. RES. COUNCIL) 1947 Dec. v 6 225-9 Bacteriological Examination of Stools for *Vibrio cholerae*

Laboratory workers in Great Britain will at least have to be prepared to recognize the true cholera vibrio in view of the possible introduction of the disease. Chronic carriers probably do not occur and the vibrio is not usually demonstrable for more than five days after onset. Attention will therefore be paid to the possibility of arrival of a patient suffering from the disease or a transitory healthy carrier who may possibly be in the incubation stage. Stools should be examined early and if delay occur should be suspended in the borate-saline mixture of VENKATRAMAN and RAMAKRISHNAN [this Bulletin 1942, v 39 458]. Direct cultivation is recommended on desoxycholate citrate agar and Aronson's medium, while Read's bismuth-sulphite modification of Wilson and Blair's medium may be used for enrichment. An inoculation intra-peritoneally of a loopful of an 18-hour peptone-water culture of the recently isolated vibrio should kill a young guinea pig in 24 hours, which distinguishes it from the non-cholera vibrios, except *V. mitsukurini* and the El Tor vibrio. No organism from a sporadic case of cholera in Great Britain should be identified as a cholera vibrio unless it is morphologically and culturally typical, falls into Heiberg's fermentative Group I, is cholera-red positive and Voges-Proskauer negative, fails to form a soluble haemolysin for sheep or goat red blood corpuscles and is agglutinated by an antiserum prepared against the specific O sub-group I of Gardner and Venkatraman. *W F Harvey*

ADISHANKAR R. PANDIT C G & VENKATRAMAN K V Statistical Evaluation of Anti-Cholera Inoculation as a Personal Prophylactic against Cholera and its Efficacy in the Prevention and Control of Cholera Epidemics. *Indian J Med Res.* 1947 July v 35 No. 3, 131-52, 1 map & 1 graph.

As is the case with many if not most, prophylactic field operations there is, statistically, the question of selection to be considered in assessment of the value of the data presented. There appear to be doubts about the effective exposure to the disease being identical in the case of the inoculated and uninoculated populations. Other considerations may cause difficulty in getting material for study even though total numbers may be large. Here for example the inquiry was contemplated only after thousands of inoculations had already been done and the test epidemic had become widespread. The vaccine used was almost invariably administered in single dose 1 cc. of vaccine containing 8000 million vibrios. The data required are (1) those pertaining to anticipatory inoculation which was taken to be inoculation done during the first outbreak in a village with respect to the second and subsequent outbreaks (2) the duration of the immunity conferred by inoculation (3) the influence of mass immunity on the occurrence of subsequent outbreaks. The investigation relates to rural areas only and the units were villages and

hamlets. A full statistical analysis has been carried out relating to 1.18 million persons in 2,350 villages who were inoculated with a vaccine containing both Inaba and Ogawa types of cholera vibrio. Altogether, in this very large scale operation, some 12½ million persons were inoculated. Of these there were recorded '1,118 cases of cholera amongst 709,977 protected persons in the inoculated population and 34,336 cases of cholera in 2,119,568 uninoculated persons. Two or more outbreaks of cholera occurred in 627 out of 2,350 villages.

In the second and subsequent outbreaks 6,589 cases of cholera occurred in the uninoculated group and 241 in the 'protected' group. That is the incidence in the uninoculated was 14.2 times greater than in the protected group. The other answers to the questions originally posed are that 'the immunity conferred by anti-cholera inoculation lasts for a minimum period of six months and probably remains effective up to 12 months' and 'Herd immunity seems to play an important part in preventing multiple outbreaks in a locality during an epidemic.' *W. L. Harey.*

CHEEMA SENGU C. Statistical Assessment of the Efficacy of Anti-Cholera Inoculation from the Data of 63 *Cases* in South Arcot District. *Indian J. Med. Res.* 1947 July v. 35, No. 3 153-70 3 figs. Appendix 171-6.

Evidently the data collected by AMBESHA S. PANDIT and ANSUKARAMAN (see previous abstract) were not wholly satisfying and an endeavour is made by the present author to study the facts for a more homogeneous population. For this he uses a smaller unit, the *Cases*, than the village or hamlet. It is a compact block inhabited by the depressed classes, who are of the same social state, live close together, use the same water supply and eat the same food. Attention was concentrated on one district only and the definition, as before, of a second outbreak was 'one which took place at least 30 days after the first'. The result of this more searching statistical analysis seems to have been a reduction in the difference exhibited by inoculated and uninoculated.

The attack rate in the not inoculated population was found to be 2.4 times that in the inoculated population. Statistical test indicated that inoculation against typhoid was not the cause and was useful as a partial prophylaxis. Although the average resistance of the population was increased by inoculation, there was no significant difference between the case-fatality rate against the attack of the inoculated and not inoculated populations. *W. L. Harey.*

New Delhi, despite the difference in the incidence of amoebiasis. It is concluded that these moderately severe diarrhoeas are not necessarily amoebic in origin and that the incidence of amoebiasis of 20 per cent. is probably coincidental. It is also suggested that pathogenic bacteria, and those that may possibly be so may play an important role in determining a person's resistance to amoebic infection and may also constitute an accessory factor in determining the power of penetration through the intestinal mucosa by *Entamoeba histolytica*.

P. Manson-Bahr

BOWTICK W. JOHNSTONE H. G. & ANDERSON H. H. Amoebiasis—Pathology, Diagnosis, and Recent Developments in Therapy. Reprinted from *California Med.* 1947 Oct. v 67 No 4 4 pp.

SCHUUR, T. E. Bijzondere vorm van coecale amoebiasis. [An Unusual Form of Cecal Amoebiasis.] *Med. Weekblad. Batavia.* 1947 Nov No 16, 306.

BINGHAM, J. A. W. Perforation of the Colon in Dysentery. Two Cases of Recovery after Operation. *Lancet.* 1948, Jan. 4 139-40.

Two cases of perforation in dysentery recovered after operation—one was an amoebic case, treated by colectomy, and the other a Flexner's bacillus infection treated by drainage of a pelvic abscess.

BOCK, H. E. Lebervergrößerung bei oder infolge Lambliosis und Amoebiasis. (Zugleich ein Beitrag zur Frage der parasitär-enterogenen Hepatopathie und der Amöbenhepatitis.) [Liver Enlargement from either Giardiasis or Amoebiasis.] *Alta Woch.* 1947 Mar 1 v 24-25 No. 21/22, 331-7 5 figs. [24 refs.]

In this rather discursive communication it is difficult to distinguish the main object. There appears to have been some doubt in the minds of German diagnosticians between the hepatomegaly of infective and amoebic hepatitis. As Giardiasis cysts were found in 8 per cent. and *E. histolytica* in 8.5 per cent. of the cases of liver enlargement considered, it was possible that in some there was a double infection.

The author claims that the early stages of amoebic hepatitis can be recognized by a positive Takata reaction as well as by vacuolation of the hepatic cells in material obtained by liver puncture. Additional evidence is afforded by increased blood sedimentation rate, leucocytosis with a shift of the Arpeth index to the left, in addition to hepatomegaly.

Response to the therapeutic action of emetine is very suggestive of the diagnosis of hepatic amoebiasis, but apparent cure may be deceptive and abscess formation may occur after it. Three instances are recorded in which after apparent satisfactory response to emetine therapy all ascertainable signs and symptoms (with the exception of a positive Takata reaction) disappeared and yet an abscess cavity was proved to exist by hepatic aspiration.

P. Manson Bahr

BANKER D. D. Amoebic Abscess of the Liver. *Indian Physician* 1947 Nov v 8 No. 11 254-62

This paper comprises a study of 130 cases of amoebic abscess of the liver seen during a period of ten years up to December 1944 and 66 cases diagnosed at autopsy. Making allowances for 12, which were included in both series, grand



total of 184 cases is obtained. Only those have been included in which confirmatory evidence was obtainable by the demonstration of typical liver abscess pus. Approximately one case in every 1,000 admitted to the K E M Hospital in Bombay turned out to be a liver abscess.

Once more a marked preponderance of the disease in the male is evident. Of the 130 patients, 97.7 per cent were males, and this is in accordance with the observations of workers elsewhere. In the present series there is no record of cases in infancy or childhood. On the other hand, the minimum age was 18 and the maximum 62, and the maximum incidence lies between the ages of 30 and 50 years. The greatest incidence was amongst the poor labouring classes.

Previous attacks of "dysentery" were recorded in 40 per cent. In 3 per cent only did dysenteric symptoms coincide with liver abscess, in the great majority, the interval between them was from 2 months to 5 years. It was not possible to record previous attacks of amoebic hepatitis. Pain in the right hypochondrium was present in 65 per cent of cases and the most prominent symptoms were pain and swelling in the same area. Shoulder pain, ocular icterus and persistent hiccough were exceptional. The commonest sign was tenderness in the right hypochondrium in 95 per cent. Enlargement of the liver was verified in 83 per cent.

Radiological screening of the diaphragm was carried out in 27 and raising of the right dome and immobility was demonstrated in all. In one only was a central circular dense area suggestive of an abscess cavity demonstrated. In 86 per cent the leucocyte count was above 10,000 per cmm.

As regards the abscess contents in 78 per cent the pus was typically chocolate-coloured and in the remainder brownish yellow. Trophozoites of *E. histolytica* were seen on two occasions only.

Two chief lines of treatment were carried out. (1) One or more aspirations combined with emetine injections. In all, 75 cases were thus treated and in 30 aspiration had to be repeated. (2) Incision and drainage combined with emetine injections were carried out in 32. In 27 cases the approach was trans-thoracic with rib resection, in the remainder it was trans-abdominal. The case mortality for all treatments was 29 per cent, but for aspiration and emetine it was 13.3 per cent. Where the abscess had perforated the mortality was higher—in 14 such cases, 10 proved fatal. After open operation in 32 cases there were 9 fatalities.

Relapses were recorded in 6 per cent.

**Complications.** Perforation was most frequent and was fatal in 71 per cent of cases [already shown as 10 out of 14].

Perforation into the right lung occurred in three, two of which healed spontaneously. Into the peritoneal cavity there were four of which three proved fatal. There were 4 perforations into right pleural cavity (three fatal) and one fatal perforation involving peritoneal and right pleural cavities together. Perforation of the abdominal wall occurred in two cases, both of which were fatal.

In six cases, secondary infecting organisms were isolated.

In 22 cases out of 66 at autopsy more than three abscesses were seen in each, in the remaining 34 (52 per cent) the abscess was solitary.

The largest abscess was 18 cm in diameter, four of them were small, being less than 1 cm.

Concurrent amoebic ulcers in the large intestine were found in 51 cases at autopsy, in the other 15 no such lesions were seen.

In 24 cases, the whole of the large intestine was involved. The caecum alone, the caecum and ascending colon and the ascending colon alone were each involved 8 times, and the pelvic colon and rectum three times. Concurrent

ulcers were more common in the proximal portion of the intestine and this coincides with the universally held view that amoebic liver abscess is more likely to occur in the right than in the left lobe. The cause of death ascertained at autopsy was perforation in 21 cases, extensive destruction of the liver in 14, perforation of amoebic ulcer in the intestine in 6, secondary lobar or bronchopneumonia in 6, and active pulmonary tuberculosis in 4. *P. Manson-Bahr*

RASTRERO R. & MENDOZA LEMASTER, A. Infecciones amebianas confundidas con cáncer. Amibiases del cuello uterino y vagina diagnosticada como cáncer uterino anizado. Amibiases de la vulva. [Amoebic infection confused with Cancer of the Cervix Uteri and the Vulva.] *Rev. Facul. de Med. Bogotá*. 1947 Sept., v. 16, No. 3, 914-20, 4 figs.

AMADOR, M. Uremia extrarenal causada por *Endamoeba histolytica*. [Extrarenal Uraemia due to *Endamoeba histolytica*.] *Medicina*. Mexico, 1947 Nov. 25 v. 27 No. 544, 515-21. [19 refs.]

Much of this article is taken up with redundancies, recording matters generally known, such as the physiology of protein metabolism, the function of the liver in the formation of urea, the history of *E. histolytica* and its cultivation, Craig's recording of the presence of nephritis in fatal cases of amoebic dysentery in the Philippines in 1904. Apart from all this, the author's thesis appears to be that *E. histolytica* needs an alkaline pH, and NaCl for its development in the body; that living in the large intestine the parasite is subjected to a varying pH according to the food taken and the intestinal flora, that a meat diet renders the faeces alkaline and so facilitates the metabolism of the amoeba, and that increased call is made on the liver to exercise its rôle of detoxicant.

In a case detailed the patient had been dying for 12 years on account of supposed renal disease and a threatened uraemic state. His blood urea was 40 mgm. and had been 75 mgm. and diet practically meatless had little effect on it; chlorides in the blood were below normal. Cysts of *E. histolytica* were found in the faeces. He was given specific treatment with carbarsone and later was eating meat daily. The blood urea fell to 23.07 mgm. and his blood pressure from 210/110 to 150/90.

The author concludes that the hyperazotaemia in chronic amoebiasis results from preceding deficiency of chloride, and is not the result of disturbance of renal function or pathological changes in the kidneys.

H. Harold Scott

BEDJAMOU E., ALBOU A. & LEONARDOX H. A propos du traitement de l'amibiase intestinale par l'association pénicilline-sulphaguanidine-émétine. [Treatment of Amoebic Dysentery with a Combination of Penicillin, Sulphaguanidine and Emetine.] *Algérie Méd.* 1947 Oct. v. 50 No. 8, 608-11.

The authors refer to the work of HARGREAVES [*this Bulletin* 1945 v. 42, 895] and BLANC and SAGUIER [*ibid.* 1947 v. 44, 524] on the treatment of intestinal amoebiasis with penicillin and sulphonamides in addition to emetine, as means of combating secondary infection.

They themselves have used this type of combined treatment for 3 patients in Algiers, with very satisfactory immediate results.

One patient suffered from amoebic dysentery only, the other two had in addition, bacillary dysentery and *P. falciparum* malaria respectively.

Varying combinations of the drugs were given over periods of 4 to 7 days, these included from 1 to 2 million units of penicillin, from 80 to 100 gm. of sulphaguanidine and either 0.37 to 0.58 gm. of emetine or 4 to 5 gm. of stovarsol.

The authors note that the cases of Blanc and Siguer were all severe, of a type seen in tropical climates in Algeria, on the other hand, mixed infections are not usually severe and amoebiasis responds to classical treatment it is therefore suggested that the value of a new method in these cases must be assessed on the long-range prognosis, rather than on immediate results, particularly in relation to relapses This must take into account the "*notion de terrain et de milieu*", since persons living continuously in a tropical environment where they are constantly exposed to amoebic re-infestations and secondary infections may have little chance of permanent cure these factors do not operate in Algeria, so that, with appropriately adjusted dosages, it may be that something more effective and permanent than the classical treatment may be found in the use of synergic methods

H J O'D Burke-Gaffney

GROSS, S J Treatment of Amoebic Dysentery with E B I Retention Enemas  
*Indian Med Gaz* 1947, Aug, v 82, No 8, 452-5

"Amoebiasis is an infection which is localized mainly in the colon and in the rectum Therefore, local treatment by topical application of medicines is indicated Treatment by means of small retention enemas containing E B I is suggested The results of 64 cases treated with this method are reported"

HAMMEL, L Dysentérie amibienne hystolytica et Kystes guéries en 2 jours par 2 applications, par voie buccale, d'une composition de novarsénobenzol Publication préliminaire [Oral Treatment of Amoebic Dysentery in Two Days with Novarsenobenzol] *J Roy Egyptian Med Ass* 1947, Sept, v 30, No 9, 429-39

The author says he had amoebic dysentery in 1944 He cured himself by taking Novarsenobenzol orally for two days He details his reactions to his treatment, but does not state the dosage he employed nor the nature of the substances he added to "detoxicate" the drug He similarly treated fifteen other cases of the disease for two days, fourteen of them, he says, successfully He hopes to obtain cure with a single dose of his preparation A R D Adams

BASNUEVO J G & SOTOLONGO F Cloroquina y acetoxifenil en el tratamiento de la giardiasis infantil [Chloroquine and Aceto-Xifenil in the Treatment of Giardiasis in Children] *Kuba Habana* 1947 Nov, v 3 No 11, 245-9 [19 refs] English summary

[See also this *Bulletin* 1947, v 44, 585 663]

KUPKA, E & NOTHHACKSBERGER, W Ein Fall von *Balantidium minutum* (Schaudinn) [A Case of Infection with *Balantidium minutum*] *Wien Klin Woch* 1947, Dec 5, v 59, No 48, 800, 2 figs

The case described is that of a woman 56 years of age who fell ill with dysentery which was treated as ulcerative colitis After two months' illness, a stool examination revealed a ciliate which was identified as *Balantidium minutum* The patient was treated with injections of quinine in 1 per cent solution and with yatren A subsequent examination revealed no ciliates The ciliate is well described in the paper and is illustrated by two figures Numerous division forms were present and the ciliate was still alive after six days at laboratory temperature [This description, and particularly the figures, show clearly that the organism is not a species of *Balantidium* but is undoubtedly *Balanthophorus minutus*, which WATSON [this *Bulletin*, 1946, v 43, 382] has shown to be the coprozoic ciliate repeatedly described as *Balantidium minutum*]

C M Wenyon

## RELAPSING FEVER AND OTHER SPIROCHAETOSSES

CHORINE V & COLAS-BELCOUR, J. Perte du pouvoir infectant des cultures de *Spirochaeta hispanica* pour l'*Ornithodoros erraticus* son vecteur dans la nature. [The Loss of Infectivity of Cultures of *Spirochaeta hispanica* for *Ornithodoros erraticus* its Natural Vector] *Bull. Soc. Path. Exot.* 1947 v 40 No. 9/10 383-8. [11 refs.]

The study of cultures of *S. hispanica* has shown that there is a gradual diminution in virulence as the number of passages increases, but this diminution is less evident in rodents than in human subjects. Even after 80 passages, 0.01 cc. of a culture will infect a guinea pig although the incubation period is increased from 2 to 14 days and the resulting infection is benign.

Various lots of *Ornithodoros erraticus* were fed through artificial membrane on suspensions of the culture spirochaetes and after varying intervals allowed to feed on normal guinea pigs. In addition ticks were ground up and inoculated into other guinea pigs. The results were uniformly negative, neither infection nor immunity being shown by any of the animals. Finally ticks were fed on rabbits that had been inoculated intravenously with 75 cc. of a rich culture of spirochaetes, immediately before the experiments. These ticks also gave negative results when tested for infectivity.

The results show that in culture *S. hispanica* loses its infectivity for the transmitting host before its power of infecting vertebrate hosts. The authors consider that this resembles the loss of infectivity to the transmitting host shown by certain strains of *Protozoa* that have been maintained artificially in the laboratory by passage in the vertebrate host without the intervention of any arthropod vector. Various trypanosomes after a certain number of passages lose their infectivity for *Glossina*; certain strains of *Plasmodium vivax* after being maintained for some years by inoculation from one human patient to another lose their power of developing in *Anopheles*; finally *Thalassidroma disper* after passage in bovines for 6 years will no longer develop in the intermediate host *Hyalomma marginatum*.  
E. Hinde

DEBBOF. Typhus récurrent et rougeole. [Relapsing Fever and Measles.] *Cahiers Méd. Union Française Algérie*. 1947 June 2, No 11 457

Report of case.

JERSON W F. Economic Control of the Relapsing Fever Tick in African Houses. [Correspondence.] *Nature*. 1947 Dec. 20 874.

*Ornithodoros moubata* is alarmingly abundant in many townships and labour camps in East Africa. It is markedly resistant to the common insecticides and its control has hitherto proved uneconomic.

The author, who is an entomologist in the Tanganyika Territory Agricultural Department, has been impressed with the outstanding toxicity of hexachlorocyclohexane to *O. moubata* and has had very promising results in practical trials with a number of Gammaxan formulations.

In laboratory tests the lightest dusting of individual ticks with 0.5 per cent. Gammaxan caused them to lose co-ordination of leg movements in 4 to 8 hours and to lose up to 10 per cent. of body weight in 24 hours by loss of fluids. Immobility apart from feeble but persistent leg movements, occurred in 12 hours to 5 days according to age and 80 to 100 per cent. mortalities resulted in 8 to 10 days. Adult ticks especially gravid females, showed leg movements up to 2 months after treatment but all eggs laid failed to hatch.

Dusting with 5 per cent DDT is slower and less effective, but mortalities of 50 to 80 per cent were obtained after more than 20 days

In the field, 0.5 per cent Gammexane dust was most economic when applied, with a simple shaker such as a round tin, to the floors and first few inches of the walls of infested houses, the application was made at 3 to 4 lb of dust per 1,000 sq ft of surface. Results were checked by five "boys" who searched the floors to a depth of 1½ inches at random for 5 minutes. In this way, infestation in a labour transit camp was reduced from an average of 20 per unit sample to less than 0.2 over a period of nine months, after this period, further treatment was necessary, possibly because of regular re-infestation from transit labourers. When the commercial dust concentrate (2.5 per cent Gammexane) was diluted with a local diluent (preferably a light diatomaceous earth, "Diatomite"), the cost of the material was about 4.5 pence per lb which is well within the economic range for large-scale use.

Extended experiments have been started in a whole township of about 1,200 houses half of them are infested with *O. moubata*, with a consequent high incidence of relapsing fever the reduction of ticks is already appreciated, although it will be some time before the relapsing fever statistics can be assessed.

It is added that this treatment has been officially standardized in several Government departments in Tanganyika as an advance on any previous control measures [see also this *Bulletin*, 1947, v 44, 1070]

H J O'D Burke-Gaffney

LING, C C A Preliminary Study of the Treatment of Chinese Louse-borne Relapsing Fever with Penicillin *Chinese Med J Shanghai* 1947, July-Aug, v 65, Nos 7/8, 225-30 [10 refs]

"A preliminary study of two cases of Chinese louse-borne relapsing fever treated with penicillin was made. It was found that penicillin given late in the paroxysm did not shorten the duration of the paroxysm, but prevented relapse and effected cure. When penicillin was administered on the first day of paroxysm, a rapid induced crisis resulted. The arbitrary doses employed were 960,000 and 1,780,000 units, and both were found to be adequate to eradicate the infection. The indications of penicillin therapy in relapsing fever are briefly outlined."

## YAWS

ARJE, S L Yaws treated with Single Massive Doses of Penicillin *U S Nav Med Bull* 1947 Nov-Dec, v 47, No 6, 965-9, 3 figs

In islands outside the Truk atoll, between October 1946 and June 1947, some 5,000 cases of yaws were treated with a single injection of penicillin. At first 200,000 units of sodium penicillin in 4 cc of sterile water was used, but later this was replaced by 300,000 units of calcium penicillin in 1 cc of beeswax and arachis oil. Cases were observed at intervals of 1-2 months for 9 months.

The total numbers of new cases and clinically active yaws were reduced, the typical secondary skin lesions were reduced to a greater extent than plantar granulomatous yaws.

This treatment was in use until adequate trained staff became available, but inadequate cold storage facilities then caused penicillin to be replaced by "mapharsen" [No serological data are reported]

C J Hackett

GUIMARÃES, F. V. Pesquisas sobre a imunidade da *Framboesia* tropical no homem. Observações feitas em 33 superinoculações e 7 reinoculações. [Immunity in Yaws: Studies of 33 Superinoculations and 7 Reinoculations.] *Mem. Inst. Oswaldo Cruz*. 1948, Dec. v 44 No. 4 649-85 6 figs. & 10 pls. English summary

This study is based upon superinoculations in 33 Wassermann-positive yaws patients and reinoculations in 7 Wassermann-negative treated yaws patients.

From 2-8 months after infection attempts at superinoculation with yaws spirochaetes were usually unsuccessful. This was independent of the presence of primary or secondary skin lesions. Treatment during this period abolished this immunity.

From 10-18 months the resistance to superinfection decreased and localized lesions resembling non-granulomatous secondary skin yaws, planicles or desquamating papular areas resulted, without generalized lesions, for at least 4 months later. This response seemed to be independent of the presence of active yaws and is not altered by treatment resulting in clinical cure and negative Wassermann reactions.

After the 5th year superinfection caused a necrotic ulcer together with an exacerbation of any other lesions present (tertiary gummatous in most of the cases studied) and swelling of satellite glands. No generalized lesions followed (in one case after 18 months). Treatment had no effect on the response. Three patients with tertiary gummatous lesions, but with yaws of less than three years' duration, did not give this response. These necrotic lesions contained only few treponemata. Their histopathology was similar to that of tertiary yaws. [In these cases the incubation period of inoculation lesions was shorter than in the previous group: 8-10 days against 20-30 days.]

Epidemiologically it is advisable to wait until the end of the generalized secondary stage of yaws before beginning treatment, since reinfection is possible but from a preventive point of view early treatment to reduce the source of infection is essential.

In yaws there is a true immunity since the response to reinfection is unaltered by treatment. This immunity is manifested by resistance or modified response to superinoculation or absence of generalization. These different immunity states may condition the different manifestations of yaws. In yaws, immunity is related to age of infection, the virulence of the organism and the individual characteristics of the patient.

[These findings are interesting and might usefully be extended.]  
C. } Hackett

## LEPROSY

DE SOUZA-ARAÚJO, H. C. & ROSKILL, C. S. C. Isolamento de bacilos ácido-alcool resistentes das águas dos efluentes das fossas OMS do Sanatório Padre Bento (S. Paulo) e do Hospital-Colônia Curupaity (Distrito Federal). [Isolation of Acid-Alcohol-fast Bacilli from the Effluents of a Sanatorium in São Paulo and a Hospital in the Federal District.] *Mem. Inst. Oswaldo Cruz*. 1948, Dec. v 44 No. 4 763-71 3 figs.

The authors obtained samples from the drainage effluents of the Leprosarium Padre Bento São Paulo, and from the drainage effluents of the Leprosarium Distrito Federal. The samples had been collected after the effluents had been treated by the Petroff method. After centrifuging, the deposits were again thrice centrifuged, the

deposit washed and sown on Loewenstein's medium Smears of the deposit showed bacilli which were acid- and alcohol-fast Several weeks later, growth was obtained which appeared to be identical with those which have been described as having been isolated from leprosy material In an addendum, Dr Roßsell records isolating the same (or a similar) organism from the effluent of another leprosarium in South Minas [see this *Bulletin*, 1945, v 42, 566, 1006]

H Harold Scott

IGNACIO CHALA H, J Comentarios sobre clasificación de la lepra Manifestaciones dermatológicas y nerviosas del tipo tuberculoides [Remarks on the Classification of Leprosy Cutaneous and Nervous Manifestations of the Tuberculoid Form] Reprinted from *An Soc Biol Bogota* 1947, May, v 2, No 6, 216-28, 8 figs

The author discusses the validity of the classification of cases of leprosy into lepromatous, tuberculoid and non-characteristic He describes the division of the tuberculoid type (as recommended at the Cairo Congress in 1938) into the reactional and the quiescent and describes each fully The "non-characteristic" cannot be, at all events ought not to be, considered a type in the same sense as either of the others The lepromatous patient, however, free from clinical symptoms, always harbours the bacillus in the lymph of the glands and is, therefore, a danger to the public and should never reach the class of the socially cured allowed out on parole

Among 513 patients studied, 48 (9.35 per cent) were of the tuberculoid type 206 (40.1) lepromatous, and 259 (50.5) non-characteristic The author regards, the last as undergoing an evolution stage of the disease which cannot be looked upon as a form or type of leprosy as it may evolve into one or other definite type By examination for Hansen's bacilli and by testing the Mitsuda reaction at intervals such patients can in time be relegated, he maintains, to their proper category In the true tuberculoid type, the reaction is strongly positive, in the true lepromatous definitely negative, in the non-characteristic it varies and may be negative or weakly positive

H Harold Scott

MONTISTRUC, E & CAUBET, P Anhum lépreux localisé au cinquième doigt [Anhum of the Little Finger in a Patient with Leprosy] *Cahiers Méd Union Française* Algiers 1947, Nov, v 2, No 14, 667, 1 fig

THIROUX and DELAMARRE are mentioned as having observed anhum and leprosy co-existing in the same patient [no reference is given] A photograph reproduced in the present note shows leprosy mutilations of the fingers of both hands and anhum of the right little finger The authors state definitely that "it is impossible, in this case, not to ascribe the anhum as due to leprosy", but in another place state more guardedly "leprosy may not always take part in the production of lesions like this" and conclude that anhum, goundou and perforating ulcer of the sole are not due to one single cause, but have a mixed aetiology

H Harold Scott

MONTISTRUC, E & RAGUSIN Le goundou lépreux Considerations étiologiques sur le goundou [The Aetiology of Goundou, Leprosy as a Cause] *Cahiers Méd Union Française* Algiers, 1947, Nov, v 2, No 14, 665-6

Authors are by no means unanimous in ascribing goundou to yaws, some say they see no cases in places where yaws is common and others report cases as rare in highly endemic yaws districts The present authors record a case in Martinique The patient, a woman 27 years of age, was suffering from leprosy

and showed typical goundou nasal tumours. Hansen's bacilli were present in the nasal mucosa and in biopsy material of a tubercle the W.R. was negative and no history indicative of yaws was obtainable.

They quote HUNCKBERG and BISHLER [but do not give the references] as having published an important work on osseous leprosy and say that the former mentions bony lesions of the upper jaw and of the bones of the nose. They also mention HURIVAUX as having shown to the Medical Society of Madagascar in 1930 a patient suffering from mixed leprosy with goundou-like tumours on each side of the nose which he called *pseudo-goundou* and added that the patient was "free from yaws".

H. Harold Scott

DE SOUZA ARAUJO H. C. "Ação bacteriológica da Tyrothricin" em relação às culturas de bacilos ácido-álcool resistentes isolados de leprocos e sua ineficácia como agente terapêutico da lepra humana. [Action of Tyrothricin on Cultures of Bacilli Isolated from Leprosy Patients and its Use in Treatment of Human Leprosy] *Mem. Inst. Oswaldo Cruz.* 1948 Dec., v 44 No. 4 749-81 2 figs.

Tyrothricin a mixture of gramicidin and tyrocidin obtained from cultures of *Bacillus brevis* a sporing aerobic saprophytic Gram-positive organism, has been recommended as an antibiotic, bacteriostatic and bacteriolytic, like penicillin. The author obtained a 1 per cent. solution of it in 95 per cent. alcohol and prepared numerous dilutions from it in glycerinated broth. He then set up a series of tubes, inoculated them with various cultures of acid-fast bacilli isolated from leprosy patients or insects which had been fed on them, and found it to be bacteriostatic in dilutions of 1:8,000 and 1:16,000 with different bacteria. He then proceeded to try it, intradermally injected, in cases of leprosy and four cases are reported in considerable detail day by day. Only the general results can be recorded here for those interested a study of these details should prove very informative. Tyrothricin proved to be a marked local irritant but it increased phagocytosis and local reaction was marked there was some systemic disturbance and the patient might say that it made him feel ill and he would ask to have the treatment changed. In spite of its action *in vitro* it had no curative action in these patients and did not prevent the development of fresh lepromata and nodules later nor did it bring about any regression of the disease.

H. Harold Scott

## HELMINTHIASIS

MEIRA, J. A. Esquistosomíase Mansoni. Subeifeio ao estudo de sua incidência e distribuição geográfica no Brasil. Lista bibliográfica brasileira sobre a esquistosomíase mansoni (doença de Manson-Pira) da Silva. [Schistosomíase Mansoni. Hálpe to the Study of Its Incidence and Geographical Distribution in Brazil, with a Bibliography]. Reprinted from *Arquivos Facul. de Hig. Saúde Pública U. de São Paulo* 1947 June v 1 No. 1 148 pp. [Bibliography]

This full and painstaking account of *Schistosomíase mansoni* in Brazil drives home the fact that the infestation is very widespread, is of great economic as well as of medical importance and calls urgently for more intensive measures of control. The work is divided into three main parts. The first, of an introductory nature points out in more or less general terms the gravity of the problem, the unsatisfactoriness or inaccuracy of the returns hitherto regarding prevalence and the almost universal (that is, in Brazil) presence of species of



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*Australorbis*, the chief snail host In this section, the prevalence in the different States is hunted at, the detailed accounts of each of 21 States occupies part II, which constitutes the greater portion of this work. Other hosts than *Australorbis glabratus* (*Planorbis centumetralis*) are *P. guadaloupensis* and *P. olivaceus*, a considerable percentage of which are found to harbour cercariae, in Ceará, for example, 17.9 per cent of 307 examined.

Space forbids our recording here the findings in the different States, but as an example we may deal more fully with Pernambuco, to which several pages in the work are devoted. Viscerotomy specimens were obtained from 5,202 persons in 40 localities, and 763 (14.6 per cent) were positive. The percentages varied greatly, in Jardim and Duarte Dias none was found, but only small numbers, 17 and 35 respectively, were examined, in Palmares the positives were 35.9 per cent of 114. Pontezinha, near the river Jaboaão, has a population of 1,200, 1,010 of these had their faeces examined, once only, and the percentage incidence by age [actual numbers are not stated] was under 5 years 2.7, 6-10 years 12.1, 11-15 years 30.8, 16-20 years 37.8, 21-30 years 30.7, 31-45 years 24.8, over 46 years 16.6. In Vitória, the figures were even higher. In all, 1,530 individuals were examined out of a population of 15,000 and ova were found in the faeces of 593 (38.6 per cent), doubtless more would have been found positive had more than a single examination been made. The percentages by age in this district were under 5 years 21.9, 6-10 years 45.4, 11-15 years 56.9, 16-20 years 52.9, 21-30 years 48.7, 31-45 years 30.5, over 46 years 25.0. Other helminthic infestations were common. *Ascaris lumbricoides* was found in 82 per cent of 1,151 examined, *Necator americanus* in 30 per cent of 421, and *Trichuris trichiura* in 24.3 per cent of 342. All these figures are taken from published papers and the author has a running comment on them.

According to the data investigated by the author, it has been estimated that there are nearly three million persons infested with *S. mansoni* in Brazil, but the author himself believes this to be a gross underestimate, as in the Northern States and Minas Geraes—highly endemic foci, it is true—nearly 2 million (1,817,892) have been found to be infested.

The bibliography is confined to papers published in Brazil and includes more than 350 references. [The whole work is full of interesting information and should prove useful in a few years time for gauging the results of measures undertaken to remedy the conditions now present.] H. Harold Scott

ORTELA, B. Considerações sobre a esquistosomose [*Schistosomiasis mansoni* (In Pedra Azul, Brazil)] *Brasil-Médico* 1947, Oct 4 & 11, v 61, Nos 40/41, 352-6

Infestation with *Schistosomiasis mansoni* is very common in this district. The author states that among 2,000 samples of faeces 1,280 contained the ova. From these 2,000 there should be deducted 200, as the specimens were from children under 2 years of age which were being examined for other parasites, notably *Giardia intestinalis*, and 300 others were repeat examinations. Thus, of 1,500 there were 1,280 (85.3 per cent) positive, and the author says that in certain districts careful examination, systematically carried out, would show that nearly all were infested. He gives short histories of 11 patients whose ages ranged between 5 and 70 years (the one aged 70 died) but they were all fairly typical. The treatment adopted was by tartar emetic, 1-2 per cent solution freshly prepared and diluted with hypertonic glucose for administration, starting with 0.01 gm and increasing gradually, according to the patient's tolerance, to 0.05 gm. Treatment was suspended when a total dosage of 1.0 gm was reached, and repeated after an interval of "some months". If there was

intolerance the drug foudadin given intravenously was found very serviceable. Repodral [see this *Bulletin* 1947 v 44 220] says the author is excellent but needs great care in watching for toxic symptoms [but none of the patients detailed in this account was given Repodral] H Harold Scott

SCHWETZ, J. La classification et la nomenclature des Planorbides (*Planorbinae* et *Bulininae*) de l'Afrique Centrale et surtout du Congo Belge. [Classification and Nomenclature of the Planorbidae especially in the Belgian Congo.] *Institut Royal Colonial Belge. Section des Sciences Naturelles et Médicales Mémoires* (Collection in-8°) 1947 v 18 No. 2, 91 pp. (31 refs.)

In this useful study of a collection of molluscs in the Museum of Belgian Congo at Tervueren, the classification and nomenclature of the Planorbidae are dealt with in a manner more lucid and refreshing to a layman than might reasonably be expected with such a difficult group. Any such contribution to the important subject of intermediaries of the Schistosomes in Africa, though in this case it has special reference to the species occurring in Belgian Congo must have special interest to medical officers in the Colonies. But the author is at pains to emphasize that although a knowledge of the correct classification is highly desirable in those who perforce or by natural interest must concern themselves with these disease carriers, the subject is a mine of pitfalls for the amateurs and that even the "experts" cannot agree with one another on certain questions of nomenclature. This is no reflection on the probity of the experts, but an illustration of the extreme complexity of the subject. He quotes J Bequaert in this connexion — "The Planorbidae are a very difficult group, owing to the relatively slight differences separating the genera and species, and the great variation within specific limits. One must not expect two students to agree in every case and I admit freely that I change my own opinion from time to time."

Advice to intending investigators is contained in another quotation from Bequaert — "There are several pitfalls to guard against in the study of molluscan hosts of parasitic worms. The most outstanding is the unwarranted indictment of any fresh-water mollusk that happens to be abundant in a locality where cases of fluke infections occur. It should be fully realized that carefully controlled experiments must be forth-coming before one can incriminate a given snail as harboring the parthenetic generations of a pathogenic trematode."

"After the molluscan host is established beyond doubt its correct identification may prove an arduous task. In the absence of comprehensive works on the Mollusca of most tropical and subtropical countries it is strongly recommended to submit specimens to one of the leading malacologists. In many genera of fresh-water mollusks the distinction of species is based on characters that are difficult to describe or even to illustrate. Identification has to proceed through comparison with specimens of allied species or from several localities, which can only be undertaken in one of the larger museums." J J C Buckley

SCHWETZ, J & DARTVILLE E. Recherches sur les mollusques de la bordure orientale du Congo et sur la bilharziose intestinale de la Plaine de Kasenyi, Lac Albert. (A Study of Molluscs on the Eastern Border of the Belgian Congo and of Intestinal Schistosomiasis in the Kasenyi Region.) *Institut Royal Colonial Belge. Section des Sciences Naturelles et Médicales Mémoires* (Collection in-8°) 1944, v 14 No. 2, 77 pp. 5 maps (1 folding) & 3 pls [Bibliography]

This is an account of a malacological survey along the eastern border of Belgian Congo from Lake Kivu to Lake Albert. Particular attention was given to snail collecting in the Kasenyi region on Lake Albert where intestinal

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schistosomiasis is prevalent The first part of the report contains more or less detailed descriptions of localities and habitats and an account of the species of snails found therein This is followed by a systematic list of all the species collected and a discussion on their ecology and distribution In the second part, available records of the population incidence of schistosomiasis in the Kasenyi area are considered in relation to the ecology of Planorbid intermediaries The authors' conclusions are at variance with the local belief that the disease is associated with fishing, and are supported by a comparative study of the incidence in different population groups and by the fact that Planorbids are most abundant in streams and in creeks which are not fished very much

J J C Buckley

YOLLES, T K, MOORE, D V, DEGIUSTI, D L, RIPSOM, C A & MELENEY, H E A Technique for the Perfusion of Laboratory Animals for the Recovery of Schistosomes *J Parasitology* 1947, Oct, v 33, No 5, 419-26, 8 figs

The detailed description and illustrations of the procedure in this perfusion technique, which is a modification of that of Faust & Meleney [this *Bulletin*, 1925, v 22, 468], does not lend itself to a brief account and should be read in the original

J J C Buckley

ERFAN Bey, M Bilharziasis of the Pancreas *J Egyptian Med Ass* 1940, Oct & Nov v 23 Nos 10/11 850-53

KHALIL Bey M & HILMI I S The Eradication of Bilharzia from Teftiche Wadi Kom-Ombo, Egypt *J Egyptian Med Ass* 1940 Dec v 23 No 12 965-79 8 figs on 4 pls [25 refs]

HUNTER, G W, BENNETT, H J, INGALLS, J W, Jr & GREENE, E The Molluscan Intermediate Host and Schistosomiasis japonica III Experimental Infection of *Oncomelania quadrasi*, the Molluscan Intermediate Host of *Schistosoma japonicum* *Amer J Trop Med* 1947, Sept, v 27, No 5, 597-602

Adult snails (*Oncomelania quadrasi*) were collected on Leyte from areas in which *S japonicum* infections were absent or rare, and exposed to infection with miracidia to determine (a) the number of miracidia that would produce the highest infection and survival rates in the snails, and (b) the time necessary for the production of cercariae after exposure to miracidia Information was also sought as to reproduction of snails kept in laboratory conditions

Individual exposures and mass exposures were carried out and the snails were kept under observation for 66 to 78 days, at the end of which time the numbers of surviving snails were regrettably small Individual exposures with 1 to 3 miracidia gave negative results with over 600 snails, of which only 22 survived the experimental period Exposures with 5 to 10 miracidia gave 33.3 per cent, 28.5 per cent and 16.0 per cent positives in 6, 7 and 25 snails respectively which survived from the original batch of 700 snails Mass exposures gave positives in every case in 1, 2 and 8 snails which survived from 3 batches of 909, 527 and 875 respectively There was a significant difference between the infection rates of 8.5 per cent and 62.4 per cent in snails examined before and after the 70th day, for which no satisfactory explanation is available It was thus established that the best results were obtained by exposing each snail individually to 5 to 10 miracidia and that a period of approximately eleven weeks is required for the development of the cercariae

Although the high mortality rate in the snails kept in aquaria suggests that suitable ecological conditions were not established, evidence was obtained in the form of young snails 5 months after the introduction of adult snails into the aquaria, that breeding was taking place.

J J C Buckley

PICK, F & DESCHIEUX R. La distomatose à *Watsonius watsoni* (Conyngham 1904) Stiles et Goldberger 1910 chez le papou. [Infection of Baboons with *Watsonius watsoni*.] *Bull. Soc. Path. Exot.* 1947 v 40 No. 5/8 202-11 5 figs. on 2 pls.

Infections with *Watsonius watsoni* have been recorded commonly among the Primates to which group they appear to be mainly confined as parasites and only one human case is definitely known that of Watson in a native of German West Africa in 1904 though Manson in 1908 described a patient with violent diarrhoea from whom many flukes were evacuated in the faeces and which were thought to be *W. watsoni*. DESCHIEUX (*Bull. Soc. Path. Exot.* 1940 v 33 306) recorded the infection in baboons (*P. pro. pharus*) for the first time and compared the clinical effects in these animals with those described in connexion with the human infection of 1904. To these data, Pick & Deschieux now add further observations on 10 baboons harbouring adult *W. watsoni*. In four of these there was chronic diarrhoea which terminated fatally and flukes numbering 200 to 1 000 were found on autopsy. The caecum was usually the most heavily infested part of the intestine. A detailed account of the post mortem findings in these four cases is provided. Of the other six cases, three had mild diarrhoea accompanied by daily evacuation of flukes over a period of two months and the condition cleared up after large masses of worms had been expelled in the course of one or two days.

Four stages in the disease are recognizable—a latent period, which may last a long time—a period of mild transitory diarrhoea of several months' duration with probable recovery—a period of serious diarrhoea of 2 to 3 weeks—a period of dehydration of a few days terminating in fatal cachexia.

The pathological lesions are characteristic and extend from the middle third of the ileum to the anal sphincter—they consist principally of inflammation of the serous membrane in the infected region of the ileum and oedemata, congested areas and punctiform erosions of the mucosa. They are the result of mechanical and traumatic effects due to the attachment of the flukes (by the large posterior sucker) and the production of multiple stases in the circulation of the mucosa, with all the consequences of prolongation of this action. These findings contrast with those in Watson's human case in which numerous worms were found on autopsy attached to the intestinal mucosa which was lightly congested, but not ulcerated. Death had been due to diarrhoea and inanition.

J J C Buckley

SMYTH, J D. Studies on Tapeworm Physiology. III. Aseptic Cultivation of Larval *Diphyllibothrididae* *in vitro* *J. Exper. Biol.* 1947 Dec v 24 No. 3/4 374-83, 3 text figs. & 7 figs. on 1 pl. [11 ref.]

BULSARA, S. N. An Unusual Case of Tapeworm Infestation. *J. Ass. Med. Women in India.* 1947 Aug v 33 No. 2, 44-5.

A case in an Indian woman suggesting an acute abdominal condition and relieved by passing a segment of tapeworm.

DESCHIEUX, R & POIRIER M. L'intoxication expérimentale du Cobaye par l'extract trichloracétique de *Taenia saginata*. [Experimental Poisoning of the Guinea-pig by a Trichloroacetic Extract of *Taenia saginata*.] *C. R. Soc. Biol.* 1947 Oct 141 No. 18/20 663-9

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ARCHIVOS INTERNACIONALES DE LA HIDATIDOSIS [International  
Archives of Hydatid Disease] Montevideo 1946, July, v 6, Nos 1/2, 606 pp, numerous  
illustrations

This volume consists of 24 items, 16 of which deal with the literature, clinical features, prevention and treatment of hydatid disease, and the other 8 are concerned with the biological aspects. The last 10 pages refer to the administrative aspects of the campaign against hydatid disease. There are many and varied illustrations, some of them in colour. The volume contains a very great deal of information and is presented on lines similar to those of preceding volumes [see also this *Bulletin*, 1944, v 41, 949]

H J O'D Burke-Gaffney

MOREY SOTOMAYOR, G. Hidatidosis de la infancia [Hydatid in Children]  
*Rev Hosp del Niño* Lima. 1947, June, v 9, No 31, 127-47, 10 figs

Much attention has been paid to hydatid in adults but its presence in the child merits more than it has received. The author records 19 cases in the 7 years 1940-46. In 1940, there were seven between the ages of 8 and 12 years, 5 boys and 2 girls, in 5 the cyst was in the lung, in one in the liver, and in one in liver, lung and brain. The last and one of the lung patients died. In 1941 and 1942, there was one case each year, a girl of 9 years with a pulmonary cyst in the first, and a boy of the same age with one in the liver in the second, the latter died. No case was seen in the next two years. In 1945, five, 3 boys and 2 girls, 3 had cysts in the liver, 2 in the lung. One, a boy aged 11 years, with a liver cyst died. In 1946 there were again five, 3 boys and 2 girls, one, a boy of 7 years with liver and lung cysts died but a girl of 8 years with both liver and lung cysts recovered. The other three were a girl of 4 years and a boy of 5 years with lung cysts, and a boy of 9 with a liver cyst, these all recovered. To sum up. Altogether, of the 19 cases, 13 were boys, 6 were girls, there were 5 deaths, 11 had pulmonary cysts, 5 had liver cysts, 2 both liver and lung cysts, and one had cysts in liver, lung and brain. Eosinophilia was only moderate in any and might be lacking.

H Harold Scott

PRAT D. Complicaciones y secuelas del quiste hidatídico. Es la hidatidosis una afección benigna como se la ha considerado hasta ahora? [Complications and Sequelae of Hydatid Cyst] *In Facul de Med* Montevideo 1947 v 32, Nos 7/8 581-93 5 figs

CLAPHAM Phyllis A. On the Identification of some Species of *Trichostrongylus*  
*J Helminthology* 1947, v 22 No 1 37-46 32 figs

DOS SANTOS J C. Estrongiloidosis asociada a schistosomosis e a sífilis [Strongyloidosis associated with Schistosomiasis and Syphilis] *Arquivos Univ Bahia Facul de Med* 1946, v 1 227-50 21 figs on 11 pls [17 refs] English summary

BASU S N. Chronic Intestinal Obstruction due to Ascariasis *J Indian Med Ass* 1947 Aug v 16 No 11 390-91  
Report of a case

LARA, H, GAN, T M, MATIAS, M Y & REYES, A C. *Digenia Simplex* as a Substitute in the Treatment of Ascariasis *J Philippine Med Ass* 1946, June, v 22, No 6, 239-42  
The practical value of an anthelmintic drug depends on factors other than its therapeutic activity, it must be available locally in large quantities.

painful nodular swellings in 4 aching joints in 3 weakness and cutaneous manifestations each in 2 and pain in the testicles, shortness of breath and pain in the abdomen each in 1 case.

In all but one case the drug produced a leucocytosis. Before treatment, the eosinophil counts ranged from 1 to 32 per cent. [actual counts not given] 24 were above 5 per cent. There was usually an increase during treatment in two cases these were over 40 per cent., in six over 30 and in 12 over 20 per cent.

At the end of 48 hours there were no microfilariae in the night bloods of 9 patients and the microfilariae were markedly reduced in numbers in the other 17. At a subsequent examination after 8 to 53 days, half the cases were shown to be free of microfilariae. In only one case was there a relatively high count, 22 microfilariae in 60 cmm. after 75 days, but this patient had originally shown 339 microfilariae. This patient had received treatment for 4 days in all, but this was interrupted in the middle for a week, because of a respiratory infection. The results could not otherwise be correlated with the amount of the drug given.

The appearance in 4 cases of tender nodular swellings and of localized lymphadenitis proximal to the swellings is suggestive of the death of the adult worm. Additional confirmatory evidence is afforded by the strong eosinophilic reaction observed in all 4 and by the occurrence in 3 of them of a sharper rise of temperature which was also of longer duration than in the rest.

L. E. Napier

NOBLE Bertha R. Informe preliminar del estudio histopatológico de dos ojos oncocercosos. [A Preliminary Histopathological Study of the Eye Changes in Onchocerciasis.] *Bolet. Oficina Sanitaria Panamericana*. 1947 July v. 28 No. 7 598-606, 16 figs.

The author who is a specialist in the Onchocerciasis Section of the Pan American Sanitary Bureau, presents the results of a detailed histopathological study of two eyes—one was enucleated from a patient suffering from glaucoma, who was also infected with *Onchocerca* the other was obtained at autopsy from a patient also suffering from onchocerciasis.

Details of technique are given and there are 16 good photomicrographs indicating lesions of the different parts of the eye examined, which included the conjunctiva, cornea, Bowman's membrane, substantia propria, iris, ciliary body, choroid, retina, optic nerve and peri-orbital tissues.

The author concludes that the microfilariae may be found in all the tissues of the eye but seem to have a predilection for the conjunctiva—no complete microfilariae could be found in the sections, but an impression was gained that they were longer than those found in the skin.

Lesions were also found in all the tissues of the eye. The inflammatory reaction was of a chronic non-specific type similar to that produced by foreign bodies.

H. J. O'D. Burke-Gaffney

TOUMANOFF C. & LA VAX-PHUNG. Note au sujet d'un cas de gnathostomose humaine observée en Indochine. [A Human Gnathostoma Infection in Indochina.] *Bull. Soc. Path. Exot.* 1947 v. 40 Nos. 5/6 169-74 3 figs. [19 refs.]

The authors record and describe a case of gnathostomiasis (*G. spungersi*) in an Annamite woman aged 42 years, from whom an immature female worm 10.5 mm. by 1 mm. was extracted.

Before its removal from a point below the left clavicle, the site of infection had been painful and slightly inflamed and later became swollen to the size

of a pea. The following day the worm was extracted (apparently by scratching the skin with a finger nail). An erythema 15 cm in diameter subsequently formed, together with an oedema which extended upward to the neck. Both disappeared in two days after local treatment and the wound healed 8 days later.

It is remarked that the skin reaction in this case differed from those described by previous authors in that the transitory oedema occurred *after* the emergence of the worm. It is suggested that in such cases the worm might escape detection by emerging unheralded, especially at night. From the case history, the infection must have been contracted either in Indochina, in which event it would be the first recorded from that country, or in Siam 16 years ago, which would indicate an extremely slow rate of development of the parasite and a very long sojourn in the human body.

J J C Buckley

TOUMANOFF, C & NGUYEN VAN HUONG. Un cas autochtone de gnathostomose humaine observé en Indochine [An Autochthonous Case of Human Gnathostome Infection seen in Indochina]. *Bull Soc Path Exot* 1947, v 40, Nos 5/6, 174-5.

Autochthonous infection with *G. spinigerum* in Indochina, strongly suggested by the case described by TOUMANOFF & LE-VAN-PHUNG [see previous abstract], is definitely established by the present authors who describe a similar infection in a Eurasian woman of 22 years who had resided all her life in Indochina. A worm, 9 mm  $\times$  1 mm, was removed from the right lumbar region by squeezing a small irritating papule resembling a mosquito bite. Thirteen hours later, a small oedematous swelling appeared measuring about 5 cm  $\times$  3 cm, with a central depression of about 5 mm  $\times$  2 mm, which was surrounded by a narrow inflammatory zone. The blood count was as follows: polymorphonuclears 56 per cent, large and small mononuclears, 7 and 5 per cent respectively, lymphocytes, 20 per cent and eosinophiles, 12 per cent. This formula is similar to that observed in the previous case of Toumanoff and Le-Van-Phung. It is remarked also that in both cases the oedematous swelling had been transitory and occurred after the worm had been extracted.

J J C Buckley

YOUNG, May R. The Incidence of *Trichinella spiralis* at Necropsies in England. *J Helminthology* 1947, v 22, No 1, 49-60 [45 refs.] [Summary appears also in *Bulletin of Hygiene*].

The author examined 472 human diaphragms for *T. spiralis* infection by a "digest" technique which is described in detail.

The number examined for each town and the percentage found infected are as follows: —Birmingham, 194 (12.4), Wolverhampton 106 (15.1), Cambridge, 37 (5.4), Bristol, 48 (12.5), Cardiff, 56 (3.57), Llandough, 7 (14.3), Leeds, 24 (all negative), which give an average infection rate of 10.805 per cent.

Statistical analyses of the figures show no significant differences between the infection rates in sexes or in age groups, but an increase in the incidence of thick-cysted infections of long standing is apparent with increasing age. With the exception of Llandough and Leeds each of the towns furnished cadavers in which were found thick-walled calcified cysts, indicating an endemicity of considerable age, whilst unencysted larvae of recent infection were found in Wolverhampton and Birmingham cadavers. From the occurrence of infections of obviously different ages in one cadaver, it is argued that one infection does not produce permanent immunity.

Examination of 4,626 specimens of pork from Wolverhampton abattoir during 1941 and 1942 revealed no positives. Some of the pigs came from widely separated localities in England. Two of 145 rats from the Wolverhampton area were positive and nine of 116 from Penrith.

At the time of the Greenwich outbreak [DAVIS and ALLOTT *Bulletin of Hygiene* 1942, v 17 271] Argentine pork was suspected and 589 specimens were examined by the "digest" technique. All were negative. J J C Buckley

DAVIS, W. A. & CLELAND R. R. Trichinosis in Prisoners of War *Bull. U.S. Army Med. Dept.* 1947 Nov., v 7 No. 11 973-6.

This paper records an outbreak of trichiniasis at Camp Atterbury Indiana, during the second and succeeding weeks of December 1945. The symptoms were chiefly chills, fever, cough and generalized muscular pains and aches. Together with the "explosive onset" these symptoms suggested influenza and an epidemic of influenza type B had just occurred in Fort Benjamin Harrison camp near by but at camp Atterbury only German prisoners of war were affected, most of the patients had had mild diarrhoea at the onset of the illness, their illness lasted longer than influenza does, their muscular pains differed from those of influenza, several patients had extensive subconjunctival haemorrhages and eosinophilia was common. Practically all the Germans admitted having eaten raw pork or bacon and the diagnosis of trichiniasis was confirmed by positive skin tests in all the 20 patients thus examined.

The infection was traced to canned bacon intended for overseas shipment and to canned pork, both issued on Dec. 7 1945. The Germans had been told to cook the bacon and pork, but these products were issued to them raw and were eaten so. The epidemic became manifest 9 days after the bacon was issued. Three men suffering from trichiniasis became ill before the bacon had been issued, but they admitted having eaten raw pork earlier. By December 7 1945 103 patients had been admitted to hospital and 77 others were admitted to isolation barracks with symptoms similar to those shown by patients admitted to hospital. In addition there were 409 patients with similar but milder symptoms who were kept in their quarters. The diagnosis of these two latter groups was based on clinical symptoms only because of lack of sufficient laboratory facilities. The authors briefly discuss the prevention of trichiniasis and refer to literature most of which has been abstracted in this *Bulletin*.

G. Lepage

VEGENTE A. FARGUEBAUM J. PIRES T. ROMAN J. DOMOSO R. HORCHER, G. BENCIO D. AGOSIN M. CHRISTEN R. SOTOMAYOR D. R. SILVA C., R. & VILCHES R. Epidemia de triquinosis en la Escuela Militar de Chile. [Outbreak of Trichiniasis in a Military Training School in Chile.] *Rev. Med. Chile* 1947 Aug. v 75 No. 8 519-24 1 graph.

There were 474 students at the school and all were examined after sickness among them had been reported. Seventy-one were healthy 297 were found to be infested with *Trichinella spiralis* and 106 were "subclinical." Diagnosis was made by the high eosinophilia and positive reactions to the Bachman test. Possibly another ten were infested who were away on holiday at the time the investigation was made. The symptoms on the whole were typical but mild gastro-intestinal disturbance headache general malaise and, in some a rash, apparently petechial as it was thought at first to be typhus. Eosinophilia ranged between 0.5 and 54 per cent. The Bachman reaction was positive in 180 of the 217 in whom it was tried (82.9 per cent). Two showed electrocardiograph changes—one a simple A-V block the other anomalies of the ST segment and the T wave, pointing to myocardial damage. The source of the outbreak was traced to pork and pork sausages undercooked. The period of incubation varied between 4 and 25 days with most between 11 and 20 days.

H. Harold Scott



MACANDREW MURPHY & DAVIS E. Trichinosis presenting with Foot-Drop and Facial Palsy. *J. nat.* 1915 Jun. 21 141

## SPRUE

MURPHY, F. Outbreaks of Sprue during the Burma Campaign. *Trans. Roy. Soc. Trop. Med. & Hyg.* 1947, Dec., v. 41 No. 3 377-406. [23 refs.]

A number of papers have appeared on the unusual aspects of sprue in outbreaks among British and Indian troops in Burma. They all deal more or less with cases of the same type and with a similar environment. The subject matter bears the same flavour of perplexity: all the various observers pursue their individual methods of approach though their conclusions appear equally mystifying and inconclusive. Such a one is the present contribution. It therefore covers much the same ground but the author would explain the epidemic nature of the outbreak on dietary grounds which others for their own good reasons would discard. This contribution in particular is long and detailed and therefore does not lend itself to concise summary.

The author observed a large number of military patients—over 3 000—and describes the incipient manifestations of what is usually a particularly chronic disease. It is not surprising, therefore, that all stages of severity were encountered, but it may justifiably be concluded that the syndrome here described was indeed tropical sprue in all its various stages of development, as is borne out by the therapeutic response to liver treatment and other recognized measures. The primary aetiological factor was believed to have been a dietary deficiency of certain components of the vitamin B<sub>2</sub> complex, and in this respect the author finds himself at variance with others.

The majority suffered from a mild form of the disease, conforming to the recently described 'para-sprue' and the author advances cogent reasons against the acceptance of what is after all a spurious division and emphasizes that there is no fundamental difference between European and Indian cases. The most noteworthy variants were the watery, more frequent, less bulky stools and lower fat content, as compared with the typical sprue evacuations seen in peace time. For this the relatively short duration of the disease, the amount and nature of fatty acids and carbohydrates, the intestinal hurry and deficiency of calcium were regarded as important. The large pultaceous stool of the fully developed disease is probably the outward sign of megacolon, and is therefore a later development. Not all cases showed the same pattern. The commonest features were lethargy, muscular weakness, anorexia, flatulent dyspepsia, white diarrhoea, glossitis, anemia and emaciation.

But even in the early stages, there were abundant evidences of abnormal fat excretion. The primary causal factors were thought to be prolonged consumption of a diet inadequate in one or more components of the vitamin B<sub>2</sub> complex. It is claimed that there was a calculable deficiency of riboflavin, nicotinic acid and pyridoxine. This was borne out, in the author's opinion, by the excretion of subnormal amounts of nicotinic acid and the therapeutic response to parenteral and oral administration of crude liver extract and other vitamin B<sub>2</sub> complex preparations.

It is stated that troops subsisting on rations richer in fresh foods did not contract sprue.

[In this respect the K rations come in for some criticism. It is not stated that deficiency symptoms *per se* were due to vitamin deficiencies in these rations but that they were so monotonous that they were not eaten. The error lay in the

assumption that men could subsist on them over indefinite periods. Bacillary dysentery was rife in these jungle-fighters and approximately 10 per cent. of them developed sprue symptoms in addition for which the primary bacillary infection was held responsible.]

Secondary aetiological factors were the increased metabolic demands made by the arduous of this exhausting campaign, increased by malaria, dysentery antecedent malnutrition and anaemia, and consequent anorexia. The high carbohydrate intake in Indian cases and the excessive fats in British cases were subsidiary causes. The author's final conclusion is in support of the Stannus hypothesis (this *Bulletin* 1943 v 40 259) that sprue is primarily the expression of failure of phosphorylation of glucose and fatty acids through lack of co-enzymes which act as catalysts. These include certain unspecified fractions of the vitamin B<sub>12</sub> complex.

There was no evidence that the development of sprue was dependent on an infective agent antecedent intestinal disease or inherent metabolic error.

That these outbreaks of sprue occurred in epidemic proportions is not considered a cogent argument against the diagnosis of sprue or as supporting the hypothesis of its infective nature.

P. Manson-Bahr

LENDER, E. B. A Case of Sprue maintained on Folic Acid. *Am. J. Trop. Med.* 1947 Nov. v 27 No. 6 723-5. [12 refs.]

Folic acid in five milligram doses by mouth daily will maintain sprue in health permanently. One five milligram tablet daily may be considered the maintenance dose for even an old case of sprue.

See also p. 360 WALKER Neurologic Disturbances with Folic Acid Therapy

## HAEMATOLOGY

MACFARLANE R. G. & O'BRIEN J. R. P. in collaboration with C. G. DOUGLAS, E. M. JOSE, H. M. JOSE, R. H. MOSE, B. AMOS & P. GURICK. The Haldane Haemoglobinometer. I. Iron, Oxygen and the British Standards Institution Colour Standard. *Brit. Med. J.* 1944 Feb. 19 448-50

Samples of heparinized venous blood from 29 men and 20 women in normal health were used in an investigation of the efficiency of the Haldane-Gowers haemoglobinometer. The following determinations were made on each blood sample: oxygen capacity by the constant volume van Slyke method; haemoglobin iron determination by the Klump titanium chloride method; ultra-violet and visible absorption spectra; haemoglobin estimation with the Haldane-Gowers haemoglobinometer; British Standard Institutions (B.S.I.) standards, diluting tubes and pipettes being used; red cell count and packed cell volume. It appeared that the 100 per cent. on the B.S.I. standard Haldane-Gowers haemoglobinometer was equivalent to about 19.7 ml. oxygen per 100 ml. and to about 49 mgm. of haemoglobin iron per 100 ml. instead of the expected 18.5 ml. oxygen per 100 ml. and 48.23 mgm. iron. It also seemed that there was a sex factor in the different proportions of iron, oxygen and colour found. Further the iron content and oxygen capacity were not strictly proportional to the readings obtained with the Haldane haemoglobinometer and the spectrophotometer. Part of the discrepancy was due to instrumental and technical difficulties while part may have been due to the presence of inactive haemoglobin or non-haemoglobin iron the presence of which in larger amounts in men than in women might account for the observed sex difference. It seems



reading between 2 and 8 per cent. lower than that given by the method of van Slyke. Secondly in matching the diluted haemolysed blood against the standard in the Haldane instrument, it is very important to observe the simple precautions laid down by Haldane himself. Before discarding the Haldane haemoglobinometer for clinical use, careful consideration should be given to its many advantages. The modern carboxyhaemoglobin standards can be accurately calibrated both at the time of manufacture and subsequently during use, and they remain stable for several years. The glassware can also be calibrated accurately and any needed correction applied. In contrast to photo-electric methods, the Haldane method is little affected by slight turbidities in the final solution and unusual haemoglobin derivatives such as methaemoglobin after sulphonamide therapy can often be detected by their tint.

F. Murgatroyd

GOODALL, J. W. D. GOODALL, Hilda I. & BANNERJEE D. Folic Acid in Nutritional Anaemia. *Lancet*, 1948, Jan. 3 20-21

Ten cases of nutritional anaemia were studied in Calcutta. The criterion was severe anaemia which did not correspond to the pure iron-deficiency type; these cases represented examples of dimorphic anaemia. Four were undoubtedly nutritional macrocytic anaemia after childbirth: the patients were so weak that they were unable to stand. Their red cell counts were about 500 000 per cmm. and haemoglobin was in the neighbourhood of 2 gm. per 100 ml. They were of the type where blood transfusion is contraindicated, but since the introduction of folic acid there have been no fatalities. One patient in particular did not respond to liver and iron for 15 days but within five days from the commencement of folic acid, progressive improvement was registered.

Megaloblasts were present in the bone marrow in seven out of the ten cases. It is concluded that folic acid in 10 mgm. doses twice daily gives a rapid haematological response in nutritional macrocytic anaemia and an equally rapid improvement is noted in the diarrhoea, fever and oedema which is often present in these cases. Furthermore it is effective whether the bone marrow is normo- or megaloblastic and is superior to liver extract in these cases. It is specially recommended as a simple remedy in the nutritional anaemia of women after childbirth.

P. Maxwell-Baker

WAGLEY, P. F. Neurologic Disturbances with Folic Acid Therapy. *New England J. of Med.* 1948 Jan. 1 v 238, No. 1 11-15

In this paper the author suggests some limitations of the therapeutic value of folic acid. He studied 14 cases of macrocytic anaemia comprising 10 cases of pernicious anaemia, one of tropical sprue, 2 of non-tropical sprue and one of macrocytic anaemia after total gastrectomy. Nine cases are discussed in detail. The response to folic acid was excellent in the single case of tropical sprue and one of the two cases of non-tropical sprue and no neurological disturbances developed in these three cases.

Neurological disturbances developed or recurred in 8 of the 10 cases of pernicious anaemia. In 3 of the 10 cases glossitis either developed or was unresponsive to folic acid. The response in the patient who developed macrocytic anaemia after total gastrectomy was slow but improvement did occur: the treatment was changed to liver therapy in the later stages.

The author suggests that his observations indicate that, with our present knowledge, the use of folic acid entails definite risk of injury to the nervous system in pernicious anaemia.

H. J. O'D. Burke-Gaffney

## VENOMS AND ANTIVENENES

CHRISTENSEN, P A **Formol Detoxication of Cape Cobra (*Naja flava*) Venom.**  
*South African J Med Sci* 1947, June, v 12, No 2, 71-5

Cape Cobra venom loses toxicity, combining power and nitrogen when exposed to the action of formalin. The rate of loss of toxicity increases with increasing formalin concentration and increasing pH, and the loss is due partly to formation of toxoid and partly to destruction.

Some loss of antigenicity accompanies loss of toxicity and combining power may be completely lost after the prolonged action of formalin. Martin's broth, *per se*, is not necessary for detoxification, its action is that of a buffer and if the reaction of saline solutions of venom is adjusted to pH 7, toxoid formation proceeds normally and yields a superior product. Optimal conditions are low concentration of formalin and low pH, and under these conditions the tendency for the formation of undesirable precipitates of low antigenic value is reduced.

P Hartley

BURETTE J **La strychnine intraveineuse dans les evenimations par colubridés du genre *Dendroaspis*** [Intravenous Strychnine in Bites by Colubrids of the Genus *Dendroaspis* *Ann Soc Belge de Méd Trop* 1947 June 30 v 27, No 2 195-9]

AHUJA, M L, VEERARAGHAVAN, N & MENON, I G K **Effects of Heparin on the Action of the Venoms of some American Viperine Snakes** *Indian J Med Res* 1947, July, v 35, No 3, 227-32

"1 Experimental evidence is presented to show that heparin effectively neutralizes, *in vitro*, the blood coagulant action of the venoms of viperine snakes *B alternatus*, *B jararacussu*, *B atrox*, *B cotiara*, *B newwedii* and *Crotalus terrificus*

"2 Heparin counteracts some of the toxic effects of the venoms of *B alternatus*, *B jararacussu*, *B atrox* and *B cotiara* in experimental animals

"3 The trial of heparin as a therapeutic agent in the bites by the above-mentioned viperine snakes is suggested"

BILLMAN D E **Arachnidism, with Report of a Case** *U S Nav Med Bull* 1947 Nov-Dec v 47 No 6 975-82 4 figs [13 refs]

Report of a case resembling an acute abdominal condition.

## DERMATOLOGY AND FUNGUS DISEASES

O'BRIEN, J P **A Study of Miliaria Rubra, Tropical Anhidrosis and Anhidrotic Asthenia** *Brit J Dermat & Syph* 1947 Apr-May, v 59, Nos 4/5, 125-58, 26 pls (1 with 2 coloured sketches) & 1 text fig

As the author points out, few common tropical diseases have received less attention than miliaria rubra. This article embodies the results of two years' research embracing the clinical, histological and experimental aspects of miliaria rubra, tropical anhidrosis and anhidrotic asthenia, the subject being an

**Australian soldier** The author suggests that miliaria rubra and tropical anhidrosis represent the acute and chronic phases of sweat gland occlusion, while anhidrotic asthenia is a general metabolic disorder resulting from wide spread occlusion of sweat glands and consequent reduction in total sweat production.

Although on superficial inspection the skin appears normal as soon as the symptoms of miliaria have passed away every affected gland does, in fact, remain chronically obstructed for a long time afterwards. Close inspection of the skin involved shows keratin plugs discernible as multiple minute greyish, shining macules. After the patient has undergone severe physical effort close scrutiny reveals deep vesicles implanted within the skin—these vesicles can be seen to disappear after the person affected has rested in a cool place. With the starch-iodine technique it may be demonstrated that each of these vesicles indicates the site of an obstructed sweat duct. If anhydrous lanoline is smeared on an area of unclothed anhidrotic skin, and the subject exercised, profuse secretion of sweat occurs on this area while the rest of the skin remains completely anhidrotic. This is clearly illustrated in a photograph.

When a large portion of the covered parts is rendered sweatless, and the subject attempts physical effort in heat, anhidrotic asthenia results. This is characterized by symptoms of exhaustion, transient amaurosis, vertigo frontal headache, dyspnoea, palpitation and the sensation of heat. The author considers that some impairment of tropical adaptation results from blockage of half a person's sweat glands, and where two-thirds or more are blocked the loss of adaptation may be severe. After some experience, examination of all affected persons immediately after exercise will allow precise immediate assessment of the degree of tropical adaptation in each individual case.

The histological changes of sweat gland occlusion are illustrated by thirty-four plates, in which four stages are illustrated. Stage I shows the closure of the sweat pore as a result of the swelling and closure of the keratin ring at its mouth. Stage II shows the primary rupture of the sweat duct and the formation of the miliarial vesicle as a result of pressure built up within the obstructed sweat gland. Stage III shows the formation of a keratin plug at the site of the obliterated vesicle and Stage IV the secondary rupture of the sweat duct and the formation of the deeper vesicle of tropical anhidrosis.

The suggestion is made that sebaceous deficiency in the tropics causes a physical change in the keratin ring surrounding the sweat duct, with resultant occlusion and rupture of the duct. In the presence of lipid the keratin lamellae are softened, the ring becomes pervious again and sweating occurs. This is the author's interpretation of the result of the experiment in which sweating occurs after lanoline has been smeared on the anhidrotic skin. Treatment is therefore aimed at desquamation of the stratum corneum with 10 per cent. salicylic acid in 90 per cent. alcohol, followed byunctions of lanoline to restore the lipid deficiency.

[This is a most interesting article based on a very detailed study of miliaria rubra and its effects. The author advances an ingenious suggestion for the mechanism of its causation.]

H. T. H. Wilson

LOWENTHAL, L. J. A. Tropical Lichenoid Dermatitis. *Arch. Dermaf. & Syph.* 1947 Dec. v 53 No. 6, 963-9

"A historical retrospect of tropical lichenoid dermatitis includes a case seen by me in 1835. Attention is drawn to the absence of lesions of the glans penis.

See also p. 370 LORD & JOHNSON The Production of Dermatitis by Pyrethrum and Attempts to produce a Non-Irritant Extract.

VARELA, G & AVILA, C "Mal del Pinto" or "Carate" and its Treatment with Chlorhydrate of 3-Amino-4 Oxiarsenbenzen (Mapharsen) *Amer J Trop Med* 1947, Nov, v 27 No 6, 663-72, 4 figs & 1 map [42 refs]

There are said to be 700 000 cases of pinta in the Americas, of which 270,000 are in Mexico. The causal organism *Treponema caratatum* was discovered in 1938. It develops abundant growth "in cultures of nervous tissues of mouse embryos" (simplified technique of Dr Ponierat, Medical School of University of Texas [no details or reference given]). There is said to be no immunity to reinfection during the disease or after recovery, nor to infection with syphilis. Yaws patients are claimed to be partially immune.

The author, working at Arcelia, Mexico found 56 per cent of children of parents infected with pinta were themselves infected, while only 43 per cent of those having parents free from pinta were affected. The coloured, red, pink, blue, brown and white, lesions, or pintides are more numerous on the exposed surfaces of the body and shoulders. Palpitations occurred in 40 per cent (of 200 patients) and the blood pressure tended to be low. Other authors have reported aortic lesions in pinta and also a high incidence of positive Wassermann and Kahn reactions which did not respond very readily to treatment. No changes have been found in the cerebro-spinal fluid.

The authors gave 0.04 grammes of "Mepharsen" twice weekly to men and women for a maximum of 15 doses. Of 66 cases observed for periods up to one year, in only three had the intensity of the Kahn reaction decreased and in 60 there was some improvement in the coloured areas. C J Hackett

SILVA F Lesões pulmonares da blastomicose de Lutz Splendor-Almeida [Pulmonary Lesions in Blastomycosis] *Arquivos Univ Bahia Facul de Med* 1946, v 1 321-31 6 figs on pls English summary

Two cases due to *Paracoccidioides brasiliensis* improved by sulphonamides

DE CASTRO PALOMINO J & ALFONSO y ARMENTEROS J Abscesos hipodermicos metastasicos en un caso de cromoblastomicosis [Metastatic Subcutaneous Abscesses in a Case of Chromoblastomycosis] *Rev Sifilografia Leprologia y Dermatologia* Marianao Cuba 1947 Apr v 4 No 2 63-71 11 figs

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## TROPICAL ULCER

PINKERTON J M Tropical Ulcer, as seen in South Iran, and its Treatment with Penicillin *J Trop Med & Hyg* 1947, Dec, v 50, No 12, 243-51, 8 figs

Tropical ulcer is very prevalent in South Iran, causing much invalidism and a certain number of deaths, it is usually associated with under-nourishment and bad hygienic conditions.

The author divides his cases into two main types—Type I "simple tropical ulcer" and Type II "phagedaenic" tropical ulcer. A few cases are classified as "transitional" or as "atypical".

Type I ulcers are irregularly circular, with a rolled edge or reddish-purple colour and a base of paler exuberant granulations exuding thin sero-pus. These ulcers seldom exceed 4 or 5 inches in diameter and are usually on the lower extremity, most often in the region of the tendo Achillis or external malleolus. Cases of this type invariably show Vincent's bacilli and spirochaetes, often associated with staphylococci and sometimes with other organisms. There is

often a marked resemblance to rodent ulcer and the author excised some of his earlier cases for this reason. This type is seasonal in its incidence and occurs during the first autumn rains in November after the long hot summer. It is more common after a poor harvest.

Type II is believed to develop from Type I by infection with anaerobic gas-producing organisms although bacteriological proof of this has not been obtained. The ulcer enlarges its base becomes deeply excavated, lined by wash-leather or dark green or black sloughs, and the discharge becomes copious and foul-smelling. Spreading gangrene occurs involving fascial planes, tendons and structures with a poor blood supply. Toxaemia begins with intermittent fever and progressive anaemia, the ulcer may enlarge to an enormous size even encircling the whole limb and before the advent of penicillin amputation offered the only hope although even then gangrene was liable to occur in the stump. The bacteriology of Type II does not differ much from that of Type I. Type II hardly ever attacks the young and vigorous. There are a few ulcers of an atypical kind, often on the upper limb which are common in Europeans.

Nine cases treated with penicillin are described. The first was a case of atypical tropical ulcer 1 inch by  $\frac{1}{2}$  inch, on the middle finger of an American cook, which had followed upon a septic wound and had remained stationary for two weeks in spite of various forms of treatment. Wassermann and Kahn reactions were negative and Leishman-Donovan bodies and *Trep. pallidum* were not found. Penicillin was given by intramuscular injection in doses of 20 000 units every 4 hours omitting one dose (100 000 units in the 24 hours). This was continued for three days (300 000 units in all) and on the fourth day the ulcer was healed. The remaining cases were all in Iranians.

Case 2. Typical Type I. Ulcer four inches in diameter above the external malleolus. Wassermann and Kahn reactions negative. Penicillin, 100 000 units daily was given intramuscularly for five days with marked effect. The area, now clean was covered with a Thiersch graft which was 90 per cent. successful and three weeks later the whole ulcer was healed.

Case 3. Typical Type II. The patient had been under various treatments for 3 months with no improvement. Wassermann and Kahn were negative. Anaerobic cultures were made with negative result. The patient was very toxic and had a large foul-smelling ulcer in the popliteal region. Penicillin was given intramuscularly 100 000 units daily for five days with striking immediate effect. Within a week the condition relapsed and thorough debridement together with opening up a sinus extended to the buttock was performed, and penicillin 100 000 units daily for five days was again given. The wound was packed with saline gauze and the limb put in plaster. Twelve days later the plaster was removed and ten days after this Thiersch grafts were applied. These were only partly successful but healing was complete within a month, penicillin cream being applied locally.

Cases 4 5 6. These were Type I ulcers in young men in good condition. All received 400 000 units of penicillin in four days and recovery was rapid. Skin-grafts were applied in all, with complete success, and the patients left hospital completely healed within a month.

Case 7. This was an ulcer in the popliteal space, classed as of transitional type although the patient was already showing signs of toxaemia. 500 000 units of penicillin produced rapid improvement in the general and local condition. Skin grafting was delayed for treatment of a heavy *Bact. coli* infection, but the patient left hospital after three months with the ulcer healed.

Case 8 was transitional. A sloughing tendo Achillis was seen in upper part of the ulcer. A tentative attempt to pull out the slough without an anaesthetic failed, and 500,000 units of penicillin were given. Temporary



improvement occurred but when the drug was stopped, the ulcer began to spread again. No further supply of penicillin was available at the time and a month later the ulcer had enlarged considerably and the whole length of the slough had been removed, together with over half the tendon. A second course of 400,000 units of penicillin was given and skin grafting was possible within a week. The ulcer had healed after four months' treatment.

Case 9 Type II ulcer. A man aged 50 had been under treatment for two and a half months with progressive enlargement of the ulcer which was of enormous extent—10 by 8 inches—over the dorsum of the foot. The patient was wasted and very toxic with intermittent pyrexia. After the superficial sloughs had been removed, he was given two courses of penicillin, separated by a short interval and totalling 1,600,000 units, with dramatic effect. This case, however, proved very obstinate owing to a heavy secondary infection with *Ps. pyocyanea* and *Bact. coli*, and developed a generalized eczema, believed to be an allergic reaction to penicillin cream. The ulcer was healed in a little less than four months after commencement of treatment with penicillin.

In his summary the author observes that "Type II" ulcers, before the advent of penicillin, almost invariably caused death unless amputation was performed; that Vincent's bacilli and spirochaetes are met with in all types and disappear after penicillin treatment; penicillin proved to be specific for all types of tropical ulcer, in "transitional" and Type II ulcers, thorough débridement is an essential preliminary to penicillin treatment, and the only ill-effect of penicillin treatment was a severe allergic skin reaction in one case. [See also this *Bulletin*, 1948, v 45, 209.]

C F Shelton

## MISCELLANEOUS DISEASES

DAVIES, J N P. Pathology of Central African Natives. Mulago Hospital Post Mortem Studies IV. *East African Med J* 1947, Oct, v 24, No 10, 352-62 [24 refs.] [Summary appears also in *Bulletin of Hygiene*]

This paper continues the author's previous records [this *Bulletin*, 1948, v 45, 211] and deals with tuberculosis in Africans. He begins by referring to various differences in the type of infection and the course of the disease in Africans as compared with Europeans. Although it is generally agreed that the disease as met with in Central and East Africa is of a severe and acute type, no instances have been found of the very malignant form described in 1920 in Senegalese who had been transported to France and which followed on a primary tuberculous ulceration of the trachea and bronchi. WILCOCKS in East Africa [*Bulletin of Hygiene*, 1938, v 13, 628] found active pulmonary tuberculosis to be common and fibrotic reactions relatively uncommon. This has been the experience of many other workers.

The author divides his cases seen in Kampala into two groups (1) Those autopsied from May 1931 to May 1946, and (2) those autopsied in 1946, there being an overlap of 25 cases. The reason for this separation is that in 1946 closer observation has been made in certain aspects of the disease.

In group (1), out of 2,994 autopsies, evidence of tuberculosis was found in 11.8 per cent, and in group (2) out of 460 cases, in 18 per cent. The apparent increase in incidence was not a true one, but the result of greater interest being shown in the disease, as many fatal cases as possible were examined.

In group (1), of 354 cases of tuberculosis 86.8 per cent were pulmonary and 13.2 per cent non-pulmonary, while in group (2) the figures were 88.7 and 11.3 per cent respectively. Bone and joint affections were rare, but a high proportion showed glandular involvement.

The evidence found post-mortem suggested that in Uganda the disease is rarely of the adult "reinfection" type but is usually the result of a primary infection with formation of a Ghon focus which fails to heal and leads to dissemination. In many instances, the lungs are riddled with acute tuberculous abscesses (a condition described by the author as "pantuberculosis"). In those cases where it was possible to determine the initial focus (about a fifth to a quarter) this was in the lower lobe but in many cases this focus could not be found. The pulmonary lesions were of a very acute type, fibrotic phthisis was very rare and the picture was one of a purulent infection without cavitation but with ragged thin-walled abscesses, the sputum teeming with tubercle bacilli. Laryngeal and tracheal lesions were frequent and the same applied to tuberculous ulceration of the intestines, while military dissemination and giant cell formation were common.

In 1946, the duration of the illness was noted in 35 cases and found to average 7.7 months. Only 6 children were autopsied, the average age of 286 adults examined was 29.5 years. No cases of healed phthisis were found, but 5 chronic cases were noted. Adrenal tuberculosis was seen in one case only and renal tuberculosis was uncommon. Surgical tuberculosis while met with in the wards, was not often found at autopsy. Tuberculous peritonitis was common and the incidence of myocardial tuberculosis relatively high. A striking lesion was a general glandular form of tuberculosis, this being found in 15 cases. Every lymphatic system in the body may be involved, and in some cases there may be a close resemblance to Hodgkin's disease.

It would appear that in Uganda the great majority of cases are of the human type of infection [see CASAGRANDE, *Bulletin of Hygiene* 1939 v 14 215]. Tuberculin testing has not been carried out to any great extent in Uganda, but it may be noted that Connolly in 1941 in the Nyanza Province of Kenya obtained 28 per cent. of positives at ages 13-17 and up to 53 per cent. positives in adults. He contrasts these results with the absence of cases of tuberculosis and thinks that under conditions in the reserves the African can deal with this infection. In Uganda it appears from post-mortem findings that tuberculosis is usually "primitive" tuberculosis, and the anatomical evidence tends to show that most Uganda Africans never have the chance of being infected. When this does occur a very few develop a primary complex which they can overcome, the remainder when they do meet infection (usually by inhalation) develop a massive primary infection which may be situated anywhere in the lungs, dissemination taking place through the glands, the blood stream or by bronchopneumonic spread. The whole process tends to be rapid and death occurs without any attempt at localization. This is the clinical interpretation as well and there is no evidence of anything but a primary complex being healed.

C. F. Shelton

MAYHEW R. L. Creeping Eruption caused by the Larvae of the Cattle Hookworm *Bunostomum phlebotomum*. *Proc. Soc. Exper. Biol. & Med.* 1947 Oct. v 68 No. 1 12-14 1 fig.

While engaged in inoculating the skin of calves with third stage larvae of *Bunostomum phlebotomum* the cattle hookworm the author on a number of occasions noted the appearance of small inflamed spots between his fingers. Some of these increased to about  $\frac{1}{2}$  inch in diameter in a few hours and 2-3 days later a narrow linear tortuous eruption appeared, this extended at intervals for a few days. Later a raised vesicular line usually developed within a few hours. It might be interrupted in some places. The affected area became swollen and intensely itchy especially in the mornings. The condition usually cleared up with a scaly skin, in about a fortnight.

A typical lesion acquired in this way in 1946 is described in detail, with daily records of its development. This occurred on the interdigital surface of the ring finger and is illustrated in a photograph. Areas where hair follicles were present were not affected, so that there was no evidence that the larvae penetrated by way of these follicles.

Evidence is also given to show that, in man and calf alike, a prickling sensation was produced almost immediately after the application of the larval suspension to the skin.

The lesions correspond closely with those seen in creeping eruption caused by the larvae of the dog hookworm, *Ancylostoma brasiliense*, but in the case of the cattle hookworm, the duration of the lesion is less prolonged. In the author's experience it lasts from 1 to 3 weeks, while that caused by the dog hookworm lasts from several weeks to months.

It is also suggested that the cattle hookworm larvae do not penetrate in such large numbers. Secondary infection sometimes develops in creeping eruption, as a result of continued scratching, but no such complication was noted by the author in the case of the present lesions. It is also noted that the eruption caused by the cattle hookworm has much in common with schistosome dermatitis, but there is no migration in the latter condition.

H J O'D Burke-Gaffney

BREA C A & CANALE E C. Miasis vulvar [Myiasis of the Vulva]. *Rev Asoc Med Argentina* 1947 Oct 15-30 v 61 Nos 615/616 734-5, 3 figs [16 refs]  
Account of a case caused by the larva of *Cochliomyia hominivorax*

ROSS, S G. Preliminary Report on Fish Poisoning at Fanning Island (Central Pacific). *Med J Australia* 1947, Nov 22, v 2, No 21, 617-21

The author gives an account of 55 cases of fish poisoning under his personal observation between February 1946 and the first week of April 1947. Forty other cases were reported to him during this period, making 95 in all out of a population of 224.

The symptoms were the same as those recorded previously from the Marianas and Honolulu and may be briefly summarized here [they have been described more fully in this *Bulletin*, 1945, v 42, 592, 593, 1946, v 43, 595]. The indigenous people cook the whole fish on burning coconut husks after wrapping it in green leaves mostly pandanus or palm tree leaves, Europeans clean the fish and cook the flesh only. Symptoms of poisoning occur after either form of preparation for eating and the poison is in the fresh fish. In one instance recorded, the fish, a snapper, was caught at 3 p.m., cleaned at once and put on ice, fried at 4 p.m. and eaten an hour later by 8 persons. All were taken ill 4-5 hours after with gastro-intestinal disturbances followed by numbness and tingling in face and limbs, a sensation of intense cold when hands or feet were immersed in water at room temperature, or in the mouth on attempting to drink. The pulse was slow, 35-40 per minute and pupils contracted [reaction to light or convergence is not mentioned]. The gastro-intestinal symptoms soon cleared off, but the nervous symptoms did not disappear for a week or more and a general weakness might persist for several weeks. No fatal case is reported, but the author states that the clinical symptoms generally are becoming more severe and the nervous features more marked. So far, ten species of fish have given rise to these symptoms, the popular and local names are stated, but not the scientific names. Those mentioned are Rock cod (grey and red), Blackjack, Bonefish, Reef fish, Snapper, Greenfish, Mullet, Red Snapper and Bream. The first the Reef fish and the last-named are non migratory, the others migratory. All except the Blackjack

## ENTOMOLOGY AND INSECTICIDES GENERAL

1. MARKE Elizabeth N. Studies of Queensland Mosquitoes. Part I. The *Aedes* (Finlaya) kochi Group with Descriptions of New Species from Queensland, Bougainville and Fiji. *Univ. of Queensland Papers Dept. of Biology* 1947 July 9 v 2, No. 5 68 pp., 20 figs. [34 refs.]

d. — Studies of Queensland Mosquitoes. Part II. New Species of *Aedes* (Subgenus Finlaya) *Ibid.* July 9 v 2, No. 6, 10 pp. 3 figs.

1. In 1943 the Government of Queensland established a National Mosquito Control Committee a function of which was to institute a research programme dealing with all aspects of the mosquito problem in Queensland. This paper is the first of a series concerned with the systematics and biology of these mosquitoes.

*Aedes* (Finlaya) kochi is an efficient vector of *Wuchereria bancrofti* and several species have been confused with it. The object of the first paper is to clear up some of this confusion and it contains descriptions of the males of 4 kochi and *A. wallacei* and of both sexes of four new species (*A. bougainvillensis*, *fijensis*, *alocasicola* and *galeucicola*). There are also descriptions of the larvae of all the foregoing species and of *Aedes solomonensis* and of the pupae of all except wallacei and fijensis. There are also notes on other species and keys for the identification of adults and larvae of this group. Important morphological details are figured.

2. Two new species are described in this paper *Aedes* (Finlaya) candido-scutellum and *Aedes* (Finlaya) wallacei. H S Lemon

THOMPSON G. A. A List of the Mosquitoes of Jamaica, British West Indies. *Mosquito News* 1947 June v 7 No. 2, 78-80 [15 refs.]

CAPPELLATI, E. Lucha contra insectos y roedores, sobre todo en los puertos y aeropuertos. [Measures against Insects and Rodents in Ports and Airports.] *Bol. Salud Publica.* 1945, Sept. Dec. 3, No 10 47-53

LORD R. A. & JOHNSON C. G. The Production of Dermatitis by Pyrethrum and Attempts to produce a Non-Irritant Extract. Reprinted from *Brit. J. Dermat. & Syph.* 1947 Nov v 59 367-75.

Extracts of pyrethrum applied to the skin form one of the most effective repellents for mosquitoes and other insects. Unfortunately these extracts contain substances to which many people become sensitized after repeated applications and then an erythema or an intensely itching papular rash is produced. Among groups of 62 men and 27 women who applied a gum tragacanth cream containing a commercial extract of pyrethrum behind the ear each day for 4 to 10 weeks, 9.7 per cent. of the men and 45.9 per cent. of the women became sensitized. (The authors point out that the higher incidence in women is not statistically significant.) When sensitization developed it was general applications to the skin elsewhere produced a reaction. The factor responsible for the dermatitis does not appear to be pyrethrin itself. If pyrethrum extracts in petroleum ether are percolated through a column of fuller's earth, the dermatitis factor is more strongly adsorbed than the pyrethrins and a preparation with less of the responsible factor can be obtained. But no extracts were prepared wholly free of the sensitizing substances. V B Wigglesworth

YATES, W W & GJULLIN, C M Pre-Hatching Applications of DDT Larvicides on Floodwater *Aedes* Mosquitoes *Mosquito News* 1947, Mar, v 7, No 1, 4-6

Extensive areas bordering the Columbia River, U S A (46 N 120 W) are flooded by the seasonal rise of the river and are the site of extensive breeding of *Aedes vexans* (Meig) and *Aedes lateralis* (Meig) Plots in these areas were sprayed with a DDT emulsion (prepared by dilution with seven parts of water from stock containing 25 per cent DDT, 68 per cent xylene and 7 per cent Triton X-100) before flooding was expected Subsequently larvae failed to reach maturity over these treated areas and the authors found by experiment that an application of 3 pounds of DDT per acre will leave a residue in the soil nine months later, which is toxic to newly-hatched larvae, despite interim flooding on two occasions

R Ford Trede

INCHO, H H & DEONIER, C C Comparative Toxicity of DDT to Three Representative Species of Mosquito Larvae *Mosquito News* 1947, June, v 7, No 2, 67-70

Laboratory tests of the toxicity of DDT preparations to three species of mosquito gave the following results (taken from tables) —

DDT preparation	Concentration (p p m) of DDT to give 86 to 96 per cent kill in 24 to 48 hours of		
	<i>Culex quinquefasciatus</i> [fatigans]	<i>Anopheles quadrimaculatus</i>	<i>Aedes aegypti</i>
1 Stable suspension	0.25	0.05	0.025
2. Stable emulsion	0.25	0.05	0.017
3 Acetone-water suspension	0.25	0.05	0.025
4 DDT in fuel oil	0.5*	0.05*	0.025*
		[60 to 66.8 per cent at 0.025 lb per acre]	

\* lb per acre

It was observed that with preparations which spread equally through the body of the water, *Culex* was much more resistant than *Anopheles* or *Aedes*. This must reflect a specific toxic effect. The *Anopheles* was also susceptible to preparations confined to the surface (oil solution and also dusts) but the *Aedes* was protected by its feeding habit and therefore apparently resistant.

J R Busvine

HADAWAY, A & BARLOW, F Toxicity of DDT applied to Limewash *Bull Entom Res* 1947, Dec, v 38, Pt 3, 489-95

Glass plates were painted with limewash (of stated composition) and subsequently sprayed with DDT solutions or emulsions. Tests were also done with pieces of limewashed plaster from houses. The insecticidal effects were determined by exposing tsetse flies (*G. palpalis*) or mosquitoes (*Aedes aegypti* or *Anopheles gambiae*) to the treated surfaces for short periods, and observing the mortality twenty-four (occasionally forty-eight) hours later.

It was found that very low mortalities followed exposure to limewash treated with DDT as compared with glass surfaces similarly treated. This was not due

to chemical decomposition of the DDT for the insecticide could be recovered and identified afterwards. Also it was shown that the amount adsorbed on the lime was negligible. The loss of toxicity is due to a simple masking effect owing to the particles of inert solid covering the DDT. A similar effect occurs with DDT emulsion, but not with a DDT dispersible powder which remains on the surface of the limewash. With the last mentioned formulation, however there is a certain masking effect on a clean glass surface because of the inert diluents already present in the dispersible powder. (The one tested contained only 5 per cent. DDT.)

A few tests with a water paint containing DDT gave analogous results. Toxicity was low because of masking of the DDT which was buried in the paint. An increase of the thickness of the paint layer naturally enough, made no difference to the insecticidal effect.

J. R. BURTON

BUSHLAND R. C. Comparative Tests with DDT and Phenothiazine against two American and Three New Guinea Species of Mosquito Larvae. *Mosquito News*. 1947 Mar. v 7 No. 1 14-17

Laboratory tests were done in Florida and in New Guinea in 1944 and 1945 with various species of mosquito larvae. The insecticides were added in acetone solution to large beakers and very fine (clear) suspensions were produced, to which the larvae were added.

The DDT was lethal at rates from one in 20 million to one in 150 million, for the different species. Towards *Culex quinquefasciatus* [fatigues] *Anopheles sinensis* and *Aedes aegypti* the DDT was about fifty times as toxic as phenothiazine [thiodiphenylamine]. Towards *Anopheles punctulatus* DDT was seventy times, and to *Culex annulirostris* DDT was 150 times, as toxic as the phenothiazine.

J. R. BURTON

YOUNG E. G. Stability of Aerosol Formulations. *Soap*. New York. 1947 Nov. v 23 No. 11 116-17 152A.

In order to prevent decomposition of aerosols in metal containers it is desirable to add a small quantity of a compound which inhibits corrosion of the metal. This paper reports tests of various substances for this purpose. They were added to a normal aerosol (containing DDT and pyrethrin) and stored at 67°C. for several months with a strip of metal from the aerosol bomb container. It was found that 0.001 to 0.1 per cent. of propylene oxide, salicylal, amino guanidine or certain other compounds very greatly reduced corrosion and decomposition of the aerosol liquid. At these rates the additives were negligible in their effects on the insecticidal functions of the aerosol.

J. R. BURTON

FAY R. W. COLE E. L. & BUCKNER, A. J. Comparative Residual Effectiveness of Organic Insecticides against House Flies and Malaria Mosquitoes. *J. Econom. Entom.* 1947 Oct. v 40 No. 5 635-40 3 figs.

Some new insecticides were tested for residual contact action against *Anopheles quadrimaculatus* and *Musca domestica* with exposure of 15 to 60 minutes in small treated cages of plywood (3x3x12 inches). Mortality was determined after twenty-four hours in a clean cage. All substances (except pyrethrins) were tested at 100 or 200 mgm. per square foot. The order of effectiveness at the end of twenty-six weeks was (1) DDT (2) Benzene hexachloride (30 per cent. gamma) (3) Chlordane (4) Toxaphene and (5) DDD [Dichlorodiphenyl-dichloroethane]. The pyrethrins (at 10 and 1 mgm. per sq. ft.) with addition of piperonyl cyclohexane or piperonyl butoxide had very little residual

effect The relative toxicity of the different insecticides was the same for houseflies as for mosquitoes, but while loss of toxicity was abrupt with the former, it was gradual with the latter

The effectiveness of a selection of commercial DDT wettable powders varied considerably, though all were applied at the same rate *J R Busvine*

OKULOV, W [The Results of the Examination of the New Soviet Insecticidal Preparation, Pentachlorine Paste *Med Parasit & Parasitic Dis* Moscow 1947, v 16, No 1, 33-5 [In Russian]

The author reports promising results of tests carried out under laboratory conditions with a new Soviet insecticide "pentachlorine paste", which contains 40 per cent DDT A 10 per cent aqueous emulsion of the paste was sprayed on various objects, 10 mgm of pentachlorine per 1 cub m of surface was used On drying, the treated surfaces showed no trace of the substance applied A narrow glass ring was then attached to the treated surface Within it were placed the insects, and the ring was covered with a glass plate After a certain period of time, the insects were removed into a test tube and observations were made on their behaviour These tests were carried out with sandflies, mosquitoes, flies and bugs Sandflies and flies proved to be the most susceptible to the action of the preparation, contact during 5 minutes being sufficient to destroy them within 5-8 hours In the case of mosquitoes, contact for 50-55 minutes was required to kill them after 30-31 hours Bugs required longer contact, after which they perished in 8-15 hours The duration of contact and the interval before death increased when the insects were exposed to surfaces which had been sprayed from 10 to 45 days previously The advantages of the new insecticide are its prolonged effect upon insects, the absence of any traces of its use on the treated surface, its complete innocuousness for animals and human beings, and the small amounts required for use in dwellings [There does not appear to be anything new in the principle, which is an adaptation of DDT] *C A Hoare*

FREAR D E H & SEIFERLE E J Chemical Structure and Insecticidal Efficiency. *J Econom Entom* 1947 Oct, v 40, No 5 736-41

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## LABORATORY PROCEDURES

ROGERS E W A Colorimetric Method for the Quantitative Determination of Bilirubin in Urine Reprinted from *Bull Inst Med Lab Technol* 1947 July-Aug, v 13 No 4 55 [10 refs]

CRANDALL, B S Removal and Prevention of Fungus Stain of Photographic Negatives in the Tropics *J Biol Phot Ass* 1947, Dec, v 16, No 2, 78-80

In the tropics, photographic negatives, stored in boxes or open drawers, may rapidly deteriorate by becoming covered with fungus mycelium The problem can be solved for 35 mm film negatives by storing them with silica gel in tins which can be hermetically sealed For larger negatives this method is impracticable In the Amazon region, it was found that immersion in the standard fixing bath "hypo" for five to ten minutes cleared the stain from the negative, and that the solution acted as a fungicide Negatives so treated remained free from fresh infection for four months Negatives have been protected from

fungus infection for ten months by immersing them in a 1 in 1 000 solution of mercuric chloride immediately after washing, or in a solution of "Lignasan" containing 2-4 gm. per litre.

[Lignasan is ethyl mercuric chloride.]

G M Findley

## REPORTS SURVEYS AND MISCELLANEOUS PAPERS

MANSON-BAHR, P. *The Practice of Tropical Medicine in London. Trans. Roy. Soc. Trop. Med. & Hyg.* 1947 Dec. v 41 No. 3 289-84 1 chart 2 diagrams & 4 figs. on 1 pl.

The Presidential Address at the opening of a Session of the Royal Society of Tropical Medicine and Hygiene offers scope for a wide variety of reflections on diseases of warm climates, or for a summing up of personal experience. In the latest of these addresses, Sir Philip Manson-Bahr has chosen the latter course, and presents a series of observations on tropical diseases as he has seen them during more than a quarter of a century of practice in London. His emphasis throughout is on the unusual, the atypical, and on the need for thorough examination of each patient and for judgment when the seemingly obvious diagnosis is not quite right. The address is, in fact, an account of a series of diagnostic puzzles—it was given with the verve and liveliness characteristic of the author's speeches.

It would not be possible to abstract this paper satisfactorily and the reader is advised to study the original, and then perhaps to ponder on the possible missed diagnoses of his own experience: the tumour of the left kidney mistaken for a spleen, the high remittent temperature due to unsuspected ichtho-rectal abscess, the rectal carcinoma which is in fact an amoeboma, the cholecystitis which turns out to be sprue.

The impression left upon one member of the audience is that medical men in Britain, called upon to treat patients from the tropics, should be particularly careful not to overlook tropical diseases in differential diagnosis, and also that those accustomed to look for tropical diseases should not overlook non-tropical conditions. Medicine is difficult enough in temperate climates, but tropical conditions make it more so—yet if there were no difficulty there would be no skill or need for knowledge and judgment. Sir Philip Manson-Bahr begins his paper by referring to the supreme importance of judgment. Judgment, no doubt is a gift but it can be cultivated, and it is evident that to improve it the doctor must learn from his own experience and to do this must follow up his cases.

Charles Walcock

MANSON-BAHR, P. *The Manson Tradition. J. Trop. Med. & Hyg.* 1947 Dec. v 50 No. 12, 238-43. [13 refs.]

The Manson tradition needs no bush—but as continuity is the essence of history it requires constant renewal for each generation if its freshness is to be maintained.

To restate the tradition of the Father of Tropical Medicine no one is better equipped, in status and in qualifications alike than Sir Philip Manson-Bahr himself—for he is as closely linked to that tradition as the tradition is linked to him.

In this paper Sir Philip recapitulates some of the outstanding features of Manson's life, achievements and outlook, and illustrates them with vivid personal memories which strikingly reveal the greatness of the man and of his work.



Stress is laid on his broad approach to scientific problems ' though sometimes unorthodox according to modern conceptions, "in his hands they proved, as results have shown, to be eminently successful" Indeed, history has shown that many now classical achievements by others in the field of tropical medicine had their origins and background in Manson's hypotheses and in his "prophetic instinct"

Manson was a clinician who saw the paramount importance of preserving the clinical aspect of medicine, whatever other specialized forms it might take and he trained himself, when no others existed to train him, in those specialized fields He was, above all, a teacher but he was "no hidebound doctrinaire His outlook was broad he was well versed in literature and possessed more than superficial acquaintance with other branches of science and natural history"

Passing from Manson himself to the wider fields which he had laid open, the author corrects any impression that the wells of tropical research have been exhausted during the last six years alone, the opportunities given to many eager workers in wartime have borne great fruit examples are given of new additions to our knowledge of tropical medicine, epidemic polyarthritis, epidemic thrombo-phlebitis, kwashiorkor, tropical eosinophilia and cardiology in the tropics are mentioned, much new light has been thrown on the transmission and control of insect-borne disease, treatment and prevention have been enriched by modern methods, technique and drugs, and, especially, many preconceived theories of the physiology and pathology of well-known diseases, for example blackwater fever, malaria, cholera and heat-stroke, have been shown to be untenable

The author concludes by showing how tropical medicine, despite its great gains in wartime, has itself suffered from the ravages of war, and he enters a plea for the preservation and reconstruction of materials and means of teaching on the same high standard hitherto maintained A suggestion is put forward for the foundation of some form of organized association—the name "the Manson Association" is suggested—which would preserve the Manson tradition, voice its own views and opinions, knit more closely in fellowship those teaching and working in tropical medicine and perhaps institute a regular Manson lecture Such an organization might also institute a central pool for building up a depository of pathological specimens and other material

If the prestige of British Tropical Medicine is to be preserved in a changing world, its devotees require to be bound more closely in their common task, and for this purpose there could be no greater or more appropriate central figure around which to rally than that of the Father of Tropical Medicine himself

*H J O'D Burke-Gaffney*

**HAMBURG Tätigkeit und Aufgaben des Hamburger Tropeninstituts [Activities and Aims of the Tropical Institute, Hamburg] 36 pp 1947**

The Institut für Schiffs- und Tropen-Hygiene, now the Tropical Institute, Hamburg, was founded by Bernhard Nocht in 1900, with the following objectives in view (1) The treatment of exotic infective diseases and diseases of warm climates (2) Research on a wide basis in tropical medicine and hygiene (3) Education and instruction of doctors students, laboratory workers and others in tropical diseases, parasitology and epidemiology

In the latter years of the late war, much of Hamburg was devastated by bombs and by fire and the Institute suffered severely but it is rising, phoenix-like, from its ashes and this booklet explains what has been done for renewing its work It embraces the following sections Clinical (under Professor Nauck) helminthological (Professor Reichenow in charge), entomological (Dr Weyer), chemical (Dr Kessler), bacteriological (Dr Lippelt) pathological and virus

research (Professor Nauck) veterinary (Dr Enlgk) epidemiology (Professor Nauck). In addition there is an animal house for the usual small laboratory animals—mice, guinea-pigs, rats, rabbits, birds, cats and dogs—and later there will be accommodation for larger animals, horses, pigs, sheep, etc.

Courses of lectures are given by the various heads of departments in their different specialities. The books of the library though removed to the basement in the war were mostly destroyed by bombs and by fire, but attempts are being made to replace lost books and papers. Finally there is to be, as of old, a museum for demonstration of photographs and specimens.

The booklet gives the titles of 31 papers published from the Institute since 1945 of 25 more at present in the press and 18 in preparation. [It will take a long time and will be a difficult uphill task to bring the new Institute to the standard of the old which as older workers in tropical medicine will remember was one of the finest in the world.]

H. Harold Scott

### BOOK REVIEW

MARTINI E. *Lehrbuch der medizinischen Entomologie*. [Textbook of Medical Entomology] 3rd Edition. pp. xvi+633 322 figs. 1946. Jena Verlag von Gustav Fischer [Rm. 29]

The first edition of Professor Martini's textbook on medical entomology was published in 1923 [see this *Bullet.* 1923 v. 20 766] the second edition in 1941 and the present volume in 1946. The third edition follows a plan similar to that of the first edition (the reviewer has failed to obtain a copy of the second edition) and maintains the same high standard as a guide to those interested in the part played by arthropods in causing disease in men and animals. That a book of so considerable a size—there are about 600 closely printed pages—is no more than a guide to medical entomology is the outcome of the author's inclusion of accounts of arthropods of mainly and often solely veterinary importance the space available for the title subject is further reduced, by descriptions of the morphology and life-cycle of the parasites carried by the vectors not only during their development in the invertebrate host but also during their sojourn in the vertebrate. Professor Martini stresses in his preface the difficulties under which he laboured while writing this third edition and it is significant of these difficulties rather than a reflection on the author that he makes but little reference to important recent advances in our knowledge of medical entomology. This lack of modernity is illustrated by an examination of the bibliography where out of nearly 1,000 references the reviewer has encountered only forty-one thirty-nine of which are in German concerning papers published after 1939.

The paper used in making this book is of exceptionally fine quality and does full justice to the many excellent illustrations. The price Rm. 29 appears more than reasonable indeed, it is doubtful whether at the present time an equally well produced volume could be published in Britain at a similarly low price.

R. M. Gordon

# TROPICAL DISEASES BULLETIN

[No 5]

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CHLORINATION AND VIABILITY OF *Entamoeba histolytica* CYSTS  
By T C St C MORTON, OBE, MD, FRCP, DTM & H, KHP  
*Air Commodore Royal Air Force*  
*R A F Institute of Pathology and Tropical Medicine*

Interest in the prevention and cure of amoebiasis was stimulated after the 1914-18 and 1939-45 world wars alike. The only real advance in treatment during the recent war was the introduction of penicillin and sulphaguanidine to counteract the secondary bacterial infection of the gut. Control of the disease has not received adequate attention, probably because of the divergent views of recognized authorities on the mode of transmission. Some emphasize the rôle of water-borne infection and others stress the direct contamination of food and drink by cyst carriers. However, it is agreed that flies play an important secondary rôle as vectors between fresh human faeces and food, but the degree of importance must vary with the humidity because the higher the humidity, the greater the viability of the cysts.

ANDREWS (1934) has shown that in volunteers who scraped their fingers through faeces containing cysts, the maximum viability of the cysts was 45 minutes in those with long finger nails, and only 15 minutes in those with short. If this fact is confirmed, the food handler is only likely to remain infective for about an hour after defaecation. The routine use of soap, water and a nailbrush could reduce the time still further, and indeed completely neutralize this source of infection.

## Sources of Infection

Fresh fruit and salads which are eaten uncooked, such as grapes, lettuces, radishes etc, have deservedly acquired an evil reputation as sources of infection. Unfortunately, the time-honoured measures advocated to render them "safe" to eat savour more of a magical rite than an effective hygienic measure. Potassium permanganate achieved its reputation as a panacea because it was effective in killing the cholera vibrio in a dilution of 1/500,000 in fifteen minutes (NAPIER 1945), but even a 1 per cent. solution of potassium permanganate is not effective against the cysts of *E. histolytica* after twenty-four hours' immersion (CRAIG, 1944). Recent work indicates that after thorough washing to rid the fruit or vegetables of gross organic matter, immersion in a strong solution of bleach for half an hour should render them reasonably safe.

## Viability of *Entamoeba histolytica* Cysts

**Survival**—The length of survival of cysts is a subject of fundamental importance from the public health point of view, but it was only when cultural methods were introduced that a reliable method of testing for viability became

available. YORKE and ADAMS (1928) found that cysts in faeces always perished at room temperature within nine days. Washed cysts, in concentrated preparations in water survived for seventeen days at 0°C. and for ten days at 16-20°C. CHANG and FAIR (1940) found that cysts survived in water for ninety days at 32°F but only for 3 days at 86°F. STONE (quoted by CHANG, 1944) states that cysts from cultures were still viable after fourteen months at 32°F.

**Thermal Death Point.**—YORKE and ADAMS (1928) using the culture viability test found that the thermal death point was 50°C. (122°F). Cysts survived for thirty minutes at 45°C. but under similar conditions were killed in five minutes at 50°C. CHANG (1944) recommends immersion of fruit and vegetables, obtained from unsafe sources, for thirty seconds in boiling water. After being treated in this manner the fruits or vegetables may be freshened by placing them in the ice-box or by immersion in ice-cold boiled water.

**Chlorination.**—In 1917 WENTON and O'CONNOR stated that cysts of *E. histolytica* could resist free chlorine in water to a strength of 1/10 000 for some hours. Eosin staining was used as the criterion of death, but the fallacy of such a standard was demonstrated by CHANG (1940) who showed that cysts were found to be non-viable by the culture method even when 40-70 per cent. of them failed to take the stain. In 1944 Chang demonstrated further that even when cysts were kept at between 40° and 50°C. for four to five months after death between 30 and 40 per cent. of them failed to be stained with eosin. He postulated that while the nuclei of the cysts were no longer viable, the cyst wall might resist the infusion of dye for a long time. YORKE and ADAMS (1928) by means of cultural methods, found that cysts were killed in thirty minutes in water containing free chlorine in a strength of about 100 parts per million at laboratory temperatures of between 20° and 25°C. They found that with 21 parts per million of free chlorine under the same conditions, scanty cysts survived. LEE (1929) also using culture methods, stated that with 5 000 parts per million of free chlorine a contact period of six hours was required to kill all the cysts. SPECTOR, BATLIS and GULLANS (1934) using eosin staining as a criterion of death, found that cysts were not all killed by an initial dose of chlorine of 500 parts per million in a contact period of 48 hours. These authors also stated that chlorine was more effective than chloramines in killing cysts. GARCIA (1935) based his conclusions on the improved assumption that cysts showing disappearance of nuclei or broken nuclei and disappearance of karyosomes were dead, and that those showing only distortion

of nuclei and disappearance of karyosomes were alive. On this basis he stated that cysts in a thick fresh faecal suspension were killed in 1½ hours with an initial dose of chlorine of 3.5 parts per million while 3 500 parts per million of free chlorine were required to kill the washed cysts in the same contact period. (In the author's case a dilution of  $\text{CaOCl}_2$  of 1/100 000 expressed as chlorine was equal to 3.5 parts per million, the available chlorine present being 35 per cent.) He concluded that the killing power of chlorine is tremendously increased in the presence of large amounts of organic material, when chloramines are formed. STONE (1937) on the other hand reported that cysts of *E. histolytica* were not more resistant than *Bact. coli* to chlorine in tap water. He found that in tap water with a density of 1,975 cysts per cc. and a total organic nitrogen content of 45 parts per million, an initial dose of 4 parts per million of free chlorine killed all cysts and *Bact. coli* in twenty minutes. When the total organic nitrogen was increased to 101.25 parts per million, 10 parts per million of free chlorine were required. Cyst suspensions from washed cultures were used, and for tests of viability both eosin staining and culture methods were employed. BRADY JONES and NEWTON (1943) using raw surface water to which 20 cysts per cmm. were added, found that with an initial dose

*Chlorination and Viability of Cysts*

of 2.73 parts per million of free chlorine, cysts were still viable at the end of thirty minutes, but by multiplying the dose 2 to 10 times, only 8 cultures were positive out of 640. Of 150 cultures exposed for over 15 minutes to fifteen times the dose, none was positive for *E. histolytica*. In the positive cultures obtained after exposures of twenty minutes or more to concentrations of 2.73 to 9.83 parts per million of chlorine, the frequency of positives was haphazard and bore no relation to the amount of the dose of applied chlorine, nor to the duration of the exposure. A possible explanation for this phenomenon is that a few cysts were protected from the action of the chlorine by particles of organic matter which exerted a dechlorinating effect in small localized areas, such a phenomenon was observed by REGAN (1942) in the case of *Bact. coli* in polluted tidal waters. If such circumstance is of common occurrence, occasional survival of a few cysts may be expected under field conditions unless the water is filtered before chlorination.

CHANG and FAIR (1941), using cysts from cultures and testing viability by cultural methods, evaluated the cysticidal effect of chlorine in terms of temperature, density of cysts and pH. They found that the higher the temperature, the lower the pH value and the longer the contact period, the greater the cysticidal effect. Doubling the density of the cysts necessitated the use of a 25 per cent higher concentration of chlorine.

CHANG (1944) with a concentration of 40 washed cysts per cc and working with gaseous chlorine, an aqueous solution of chlorine, and with chloramines, carried out a very elaborate series of experiments in which the strengths of the stock solutions and of the residual chlorine were determined by the acid-starch iodide method. The pH of the chlorinated water was estimated by an electrometer and in the expectation that the oxidation-reduction potentials of the chlorinated water might show a close relation between the concentration of chlorine and the cysticidal efficiency, the voltage of the chlorinated water was determined by a brilliant platinum electrode against calomel half cell. All experiments were carried out at 18°C and nitrogenous organic matter from domestic sewage and from proteose peptone was used in varying amounts in a parallel series of experiments. In addition, studies were made to find out whether there was a penetration of chlorine into the cysts and what sort of morphological changes took place in them after chlorination. He found that with a high concentration of chlorine, such as 50 parts per million, 65-75 per cent of the cysts were stained yellow with orthotolidine, and that these yellow-stained forms were coarsely granular. He found that the entrance of free chlorine into the cysts, or of chloramines, is associated with the entrance of thought to indicate that chlorine probably combined with the proteins in the protoplasm and rendered the latter insoluble. However, in most of the tests made, the cysts were usually killed long before the chlorine was detectable in them, and before the gross changes in appearance had taken place. In several tests it was found that the death of cysts was associated with morphological changes of the nuclei. The earliest changes were splitting of the karyosome and irregularity of the nuclear membrane followed by irregular granules of the karyosome and a broken or disintegrating nuclear membrane. The most advanced stage was a total disappearance of the nuclei with irregular granules scattered in the cyst. It was apparent that the death of a cyst was brought about by the destruction of the nuclei, the first sign of which might be the splitting of the karyosome. This, according to GARCIA (1935) had postulated criterion for viable and non-viable cysts which after chlorination, was not on the basis of the morphological changes seen after chlorination, was not justified. The viability of chlorinated cysts was determined by culture methods. The cysts in each bottle were recovered by centrifugation and were placed in a

tube of liver infusion agar medium which had already been seeded with the bacterial flora isolated from a culture of the N.R.S. strain of *E. histolytica*. Chang suggests that the death of a cyst is the result of the destruction of its nucleus by chlorine—that the destruction of nucleus depends on the penetration of the chlorine into the cyst—that the penetration of chlorine into the cyst depends on the nature of the chlorine compound—and that the amount of active or free chlorine in the water depends on the hydrogen ion concentration of, and the amount of organic matter and ammonia present in, the water and also on the temperature of the water. The oxidation-reduction potential seems to give a more accurate measurement of the cysticidal or germicidal efficiency of chlorine, since it indicates the amount of active or "free" chlorine present under all conditions.

Chang found that, at a pH of 7 and a temperature of 18°C. gaseous chlorine applied for 15–30 minutes is the most powerful cysticidal agent; hypochlorite is slightly less so and chloramine the least. For long contact periods, such as 120 minutes the efficiency of all three was about the same.

In another series of experiments he showed that with a pH of 7 at a temperature of 18°C. and with a total organic nitrogen content of 0.1 to 0.19 parts per million, an initial free chlorine of 3 parts per million was effective on raising the pH to 8.5. 11 parts per million were required to kill all cysts in 30 minutes' exposure.

### Summary

The results obtained by different investigators are divergent and contradictory. On critical examination it is obvious that this divergence is due to two factors: different criteria for assessing the viability of the cysts after treatment with chlorine—and the different conditions, chemical, physical and biological (such as the density of cyst suspensions) under which the tests were made.

(a) *Viability*.—The early workers used eosin staining as a criterion of the death of cysts. Chang and Fair (1941) showed this method to be very unreliable. Cysts were found to be non-viable by culture, although 40–70 per cent. failed to take the stain. Cysts were kept at 40°–50°F. for four to five months after the period of viability as shown by culture and some 30 to 40 per cent. failed to be stained by eosin. The authors concluded that, while the nuclei of the cysts were no longer viable the cyst wall may resist staining by eosin for a long time. Similarly the morphological appearance of cysts after chlorination cannot be entirely relied upon as an index of viability. Culture methods, provided adequate controls are used, remain the only practical criterion for viability.

(b) *Varying conditions under which the experiments were performed*.—Much of the work of the early investigators is vitiated by the facts that few of them defined the conditions under which these tests were made and that they did not take into account the importance of the temperature, hydrogen ion concentration, density of cyst suspensions and amount of organic matter present in the water.

### Conclusions

Under ideal conditions as little as four parts per million of free chlorine will destroy the cysts of *Entamoeba histolytica* in water after thirty minutes. The presence of organic matter and its varying nature under field conditions, preclude sole dependence on the cysticidal properties of chlorination. This is taken into account in the sterilisation of water in the service water carts, where both filtration and chlorination are carried out.

Potassium permanganate, as a means of sterilizing fresh fruit, lettuces, etc. should be abandoned and replaced by strong solutions of bleaching powder containing at least 100–200 parts of free chlorine per million. Subsequent washing should then be done with safe water.

A level teaspoonful of good bleaching powder added to a gallon of water makes approximately a strength of 100 parts per million of free chlorine

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## SUMMARY OF RECENT ABSTRACTS\*

## IV TRYPANOSOMIASIS

## AFRICAN TRYPANOSOMIASIS

*Actiology*

FAIRBAIRN and BURTT (p 506) have studied the infectivity to man of a strain of *Trypanosoma rhodesiense* isolated in 1934 by CORSON and maintained by cyclical transmission through *Glossina morsitans*, mainly in sheep and antelopes. It is still highly infective to man and shows no sign of reverting to a *T. brucei* type. The authors have noted the fact that a fly may fail to infect a volunteer at one bite, but succeed later, or that the volunteer may be infected by one fly, but not by another, both infected from the same source. They think that the explanation of these anomalies lies in the dose of metacyclic trypanosomes ejected by the fly, and after counting trypanosomes ejected by flies attempting to feed, conclude that the minimum infecting dose for this strain is about 350 trypanosomes. The power of a strain to invade the salivary glands, and its virulence, are also factors, and the authors discuss these. Virulence and infectivity to man are separate and independent, variable qualities. The authors discuss the changes in infectivity to man that may be brought about by prolonged residence in sheep, and changes in virulence which are probably the result of mutation of genes. In comment, Corson suggests that the authors' views on the size of an infective dose may not be accepted unreservedly by some workers, and that there may be a factor of selection working on a heterogeneous strain.

In a long and closely reasoned paper, FAIRBAIRN and CULWICK (p 649) set out their views on the electrical charges of trypanosomes and the effect of these charges (positive and negative in different individual trypanosomes) on

\*The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin* 1947 v 44. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

attraction to or repulsion from other trypanosomes or red blood cells, themselves charged. The authors describe long short and intermediate forms, and report observations which indicate that syngamy occurs, trypanosomes with opposite electrical charges fusing and later dividing. This process results in a heterogeneous population. BLOOM adds a comment to his abstract of this paper—the whole subject should be studied in the original.

The same authors (p. 1051) show that a sub-strain of *T. rhodesiense* maintained by cyclical passage through tsetse and sheep remained polymorphic for 12 years, whereas another substrain, maintained (in England) by syringe passage through mice has become monomorphic. They argue that it is known that syringe-transmitted strains of the *brucei* group tend to become more sensitive to arsenicals, and that any chemotherapeutic tests should be carried out on strains which are polymorphic and which have been and are, transmitted by *Glossina*.

LEWIS and LARGRIDGE (p. 980) have studied the trypanosomes (*T. brucei*) ejected by tsetse flies from time to time after infection, and describe the course of development which these appearances suggest that the trypanosomes undergo in the flies. Details should be sought in the original.

WERNHAM (p. 1051) describes a new medium of agar and human citrated plasma and red cells, for the cultivation of *T. gambiense* and *T. rhodesiense*.

#### Transmission

SCHWITZ (p. 508) discusses the distribution of species of *Glossina* in West Africa—he thinks that this is not wholly regulated by climate and vegetation.

BREQUART (p. 294) describes the tsetse flies of Liberia. There are 4 known species of which only one *G. palpalis* is a vector of human trypanosomes. He advises on measures to control these flies by recognized methods. FERRAZA (p. 1052) contributes a note on the biology of *G. palpalis* in Portuguese Guinea, which is a confirmation of work done elsewhere.

JACKSON (p. 47) allowed *G. morsitans* to hatch from pupae in part of Tanganyika Territory in which this species does not occur and studied the flies subsequently caught. Most of these were males, and most of them had fed by the fourth day. There is good correlation between age and fraying of the wings. The average distance from the point of hatching at which the flies were caught was nearly 400 yards in the first week to nearly 1 000 yards in the fourth though some were found more than 1 000 yards away. Second generation flies were found, showing that mating had taken place. BURTT (p. 803) has previously shown that *G. morsitans* hatched from pupae incubated at 30°C. are more effective vectors than those from pupae kept at laboratory temperature but he now notes that this laboratory temperature, in East Africa, may reach 30°C. at certain times of the year. The difference is that incubated pupae remain at that temperature, whereas the others reach it only from time to time.

GLASGOW (p. 47) has observed the seasonal abundance of biting flies in Tanganyika Territory but concludes that none of them is satisfactory as an indicator species to point the way to an understanding of tsetse distribution and activity.

THOMPSON (p. 803) reports a nematode of the *Merus* type in tsetse flies.

#### Control Treatment Prophylaxis

Three Annual Reports (for 1944-46) of the Sleeping Sickness Service of Nigeria have been reviewed (McLINTOCK p. 971). The staff of this Service was reduced to a maintenance basis during the war but survey and re-survey work was continued, and protective clearing work was done on a considerable scale, so that by 1944 about 400 000 people had been protected by communal effort. Work on the Anchan tsetse free corridor was continued, on the lines of development of agricultural resources. In the mining areas, examinations of labourers



are made every 6 weeks, and the average incidence each 6 weeks was 0.67 per cent in 1945, high enough, but much lower than in 1940. The highest rates of infection found in re-surveys in 1946 ranged from 2 to 12 per cent in individual hamlets in Katsina, with an average of 2.8 per cent. In most parts of this province the figures show very great reduction over those of 1936-37. Trials of pentamidine as a prophylactic are continued, and a report is given on the trial of certain other drugs in treatment.

MORRIS (p. 51) has attempted control of *G. palpalis* and *G. tachinoides* in the Northern Territories of the Gold Coast by protective and eradication clearing. Protective clearing, for example where a road crosses a stream, entails total clearing along the water-course, a total clearing for one mile reduces fly by about 90 per cent. Eradication clearing entails permanent removal of those species of trees and bushes which give shelter to the flies, especially in the dry season. He begins at the head waters of a river system, and eliminates these trees from the whole system, working down-stream. In one area having 250 miles of river, he achieved by this method an almost (but not quite) total elimination of fly, and a great reduction in sleeping sickness and cattle trypanosomiasis, and thus opened the land to re-settlement.

VANDERPLANK (p. 804) has shown that DDT is lethal to all species of *Glossina* but that when it is applied to cattle, or to screens, its effect is greatly reduced within a few days because the crystals are brushed off by vegetation or washed away by rain. In tests with mosquitoes and tsetse flies, BARLOW and HADAWAY (p. 1053) have found that DDT and gamma benzene hexachloride are absorbed into leaves to the extent of 20-50 per cent, that on mud walls aqueous suspensions leave more effective films than solutions or emulsions, and that limewash interferes with insecticidal action, largely by physical absorption or masking of the particles. A "sticker" (sulphite lye) also masks the activity of DDT, presumably by coating the particles.

FINDLAY *et al.* (p. 406) have found some repellent action for tsetse flies in four substances, which they name

VEATCH (p. 293) reports on surveys made in West Liberia in 1941-43, when 90,980 persons were examined and 13,481 cases diagnosed, and again in 1943 in N.W. Liberia, where 32,617 persons were examined, and 2.2 per cent found infected. Much of the second area had been surveyed in the first expedition. Men were affected more often than women, and the common age incidence was 20-40 years. Only 6 per cent showed infection of the nervous system. Details of treatment with antrypol and tryparsamide are given. Good results were achieved.

VAN HOOF (p. 1048) describes the trypanosomiasis campaigns in the Belgian Congo, where each year between 2 million and 5 million people are examined, and infected persons treated. The proportion of infected has remained constant for 10 years at about 0.25 per cent, and there are general reports of an increase in cases resistant to arsenicals in some places reaching 50 per cent. The recent trend has therefore been to give more attention to prophylactic injections of pentamidine, which protects for 6 months. Arsenic-resistance probably exists in most mixed strains of *T. gambiense* and the resistant strains are selected and eventually predominate as a result of mass treatment with arsenicals. But resistant strains are not so easily transmitted as normal strains by flies [see also PÉLISSIER below]. The author thinks that malarsen oxide is useful for the treatment of patients with resistant strains (a conclusion not shared by LOURIE). Dogs, pigs and goats can be infected with *T. gambiense*, and may play some part as reservoir hosts in nature. The author failed to infect man with *T. brucei* by the bite of infected flies. He found that immunity to *T. gambiense* is of short duration in animals cured of the infection, but that there

is evidence of cross immunity between *T. gambiense*, *T. rhodesiense* and *T. brucei* but not between these and *T. congolense*.

Owing to the difficulty of completing the usual course of 12 injections of trypanamide, at intervals of one week, in patients with *T. gambiense* infection in the Gold Coast, FOWLER (p. 978) has given intensive courses of 2 gm. each day for 6-9 days, either by intravenous drip (lasting 8 hours for each injection) or by ordinary intravenous injections. The results, in a small series of patients, were reasonably good.

PALLISER (p. 975) discusses trypanamide in the second stage of *T. gambiense* sleeping sickness, in relation to dosage and to the question of arsenic-resistance. During the war supplies of trypanamide were limited, and it was therefore decided that the course should be reduced to 6 injections. The results, as determined by re-survey some four years later, were not good, and a course of 6 doses is consistently less effective than one of 12. Moreover it has been found that trypanamide is less effective now than it was in the early days of its use, probably owing to the development of arsenic-resistant strains: there is a tendency to stabilization of results because the arsenic-resistant strains are not so easily transmitted by *Glossina* as the ordinary strains. He also discusses the toxic action of trypanamide and the Jarisch-Herxheimer reaction, and the question of arsenic resistance of the patient. ERRANTIS (p. 49) gives evidence which suggests that in one area of the Belgian Congo where trypanosyl had chiefly been used, there had been a considerable development of arsenic resistance. This was later countered by a method of detecting arsenic-resistant strains and treating them with antitrypol, tartar emetic and trypanamide, but the method was difficult. He used antitrypol as a prophylactic in the uninfected population, and is enthusiastic as to its value. It apparently cleared an endemic focus.

CROCCALDI (p. 45) gives an account of the activities of the Pasteur Institute of Brazzaville in relation to sleeping sickness during 1944. Cases were discovered by mobile units and at fixed dispensaries. Trials were made of *p*-arsenosophenylbutyric acid in treatment, but the results in general, were not favourable when compared with those achieved by the older remedies. WILLIAMSON and LOURIE (p. 48) have shown that this compound acts on trypanosomes, even if resistant to trypanamide, but that if *p*-aminobenzoic acid is given before the arsenosophenylbutyric acid, the action of the latter is inhibited, probably because the PABA limits its admission into or on to the trypanosome cell. WILKINSON (p. 295) reports on two trivalent arsenical preparations in sleeping sickness in Liberia, namely melarsen oxide and *p*-arsenosophenylbutyric acid. Only a few patients were treated with these drugs.

SCHUELLER *et al.* (p. 1052) have used the method of determining the extent to which mapharsen inhibits the utilisation of glucose *in vitro* by trypanosomes, as a measure of the anti-trypanosome effect of that drug and have used strains of *T. equiperdum* of different degrees of arsenic-resistance.

PIERSON (p. 885) claims success in trypanosomiasis by treatment with silver arsenate, but does not give details of the type of infection, or the dosage used.

LEVADITI and VAISMAN (p. 186) confirm old work that fresh rabbit liver extract renders atoxyl trypanocidal *in vitro* and that glutathione and cysteine have the same effect.

SCHMITZER *et al.* (p. 185) have investigated the rôle of antibodies in the development of drug-resistance by *Trypanosoma equiperdum*. The paper is technical and the subject is complicated: details should be sought in the original.

DE BORCHGRAVE (p. 570) shows that the quinoline derivative Chinozol can *in vitro* sterilise blood infected with *T. gambiense* and that it can be used in

blood transfusion work where there is a possibility that the donor is infected. It shows little activity as a therapeutic agent.

VAN HOOFF *et al* (p 979) have shown that the protection against *T gambiense* conferred on guinea-pigs by injection of pentamidine is not increased by repeated injections of cultures of the trypanosome at intervals after the drug injection, and is therefore presumably independent of specific immunization. They consider that, in proper dosage, this drug may protect man for a period of 6 months, whereas Bayer 205 is said to be active for only 3 months, and is more toxic. They have used pentamidine on a large scale for this purpose, in a dose of 5 mgm per kilo. CLAESSENS (p 49) has used propamidine isethionate by intramuscular injection of 5 mgm per kilo of body weight, as a prophylactic in the Belgian Congo. Of 131 people so injected, one was found to be newly infected within 6 months. LAUNOY and LAGODSKY (p 702) find a correlation between the size of protective dose of pentamidine (below toxic level) and the period of protection conferred in rats against subsequent infection with *T brucei* and other trypanosomes.

#### *Clinical Findings*

LAPEYSSONNIE and LAPEYSSONNIE (p 295) report a case in which trypanosomes [presumably *T gambiense*] were found in ascitic fluid. In comment, BURKE-GAFFNEY records a similar case seen in East Africa [where the trypanosome was probably *T rhodesiense*].

HENDERSON-BEGG (p 509) has found heterophile antibodies in the serum in trypanosomiasis, although in some respects these differ from those found in infectious mononucleosis, care should be taken in diagnosing the latter disease in Africa, on the strength of this test.

COOKSON (p 975) states that in both trypanosomiasis and leishmaniasis there is excess of serum globulin and euglobulin, and that this can easily be detected by the serum-formalin test. He has used this on sleeping sickness patients and suspects, and although positive results are given in some other conditions, he regards it as a useful ancillary in diagnosis.

#### *Trypanosomiasis of Animals*

FULTON and LOURIE (p 403) have studied immunity in mice infected with *T congolense* and *T rhodesiense*, and subsequently treated with phenanthridinium or diamidine compounds. Homologous immunity was marked, with complete failure to reinfect after 20 to 26 weeks respectively, but the immunity sometimes broke down, and this may have been due to changes in the antigenic structure of the trypanosomes as they are passaged. *T congolense* is antigenically more labile than *T rhodesiense*, and lability renders the immunization of animals, or man, difficult in the field, where there are many antigenic types.

DAUZIER (p 805) discusses the immunity associated with drug treatment of certain experimental trypanosome infections. The original paper is a long thesis and an adequate summary is impossible in a small space.

A study of plasma proteins, erythrocyte sedimentation rate, potassium levels in serum and blood, and fragility of red cells during the course of infection with *T brucei*, *T equiperdum* and *T lewisi* in rats, is reported by IKEJIANI (p 572), but for details the reader should consult the original.

LAWS (p 804) find that the method of counting *T congolense* against leucocytes, in thick films, gives a reasonably accurate measure of the infection in cattle. LAUNOY and PRIEUR (p 509) show that the two phenanthridinium compounds S 897 and S 1553 are active against *T congolense*, and can be injected subcutaneously.

VAISMAN (p 981) reports experiments which indicate that, under certain conditions of infection, *Trep duttoni* attenuates infection by *Trypanosoma brucei* and *T equiperdum* in mice.

## CHAGAS'S DISEASE

TORREALBA (p. 187) has republished a series of his own papers on Chagas's disease in Venezuela most of these have already been reviewed, but together they form an extensive survey of information. SEIJAS RIVAS (p. 297) reports on Chagas's disease in part of Venezuela.

POYCE CARALLERO (p. 54) found a few cases of Chagas's disease in Bolivia, and remarks that the presence of *T. cruzi* in the blood is transient. ASCAZ TORRICO (p. 510) names 35 vertebrate hosts of *T. cruzi* and the 7 commonly infected bugs of Bolivia.

ROMANA *et al.* (p. 404) found 23 per cent. of children in one area of Argentina, positive to Chagas's disease by xeno-diagnosis, and 51 per cent. by complement fixation test.

D'AKDURAIN (p. 511) found infection in the rodent *Octodon degus degus* in Chile.

FLOCK (p. 53) in French Guiana infected *Rhodnius pictipes*, *R. prolixus* and *T. rubrofasciata* with *T. cruzi*, the two first more readily than the last. There is evidence that the local strains are more specially adapted to them than to *T. rubrofasciata*.

HAWKING (p. 1054) has cultivated *T. cruzi* in tissue cultures of rat embryo cells. Leishmania forms appear in cardiac muscle cells, and eventually complete trypanosomes are formed which become extra-cellular.

ADLER and BICHOVSKY (p. 52) have found that biotin concentrate inhibits the growth of *T. cruzi* and certain other protozoa, but the active substance is the concentrate is not biotin itself.

MUNIZ and DE FREITAS (p. 296) have found that if *T. cruzi* is washed free of all blood constituents before being inoculated into the liquid of fresh N.N.N. medium the transformation into crithidia forms which usually occurs does not take place. They have investigated the reason. The same authors (p. 571) have prepared an antigen from *T. cruzi* which is a mass of disintegrated culture forms suspended in a saline solution of merthiolate—this ensures retention of antigenic properties for a considerable time. With this, complement fixation tests have been performed and correlated with agglutinin and precipitin reactions. The tests revealed fluctuations in the immune state. Immunity shows itself early in infection, when the reticulo-endothelial system is mobilized, and increases as the blood is invaded—the development of leishmania forms is a defence against this vigorous immunity for these forms develop into trypanosomes when grown in medium lacking immune bodies. In the body antibody formation decreases when the leishmania forms predominate.

ROMANA and GIL (p. 405) describe the preparation of an antigen for use in the complement fixation test in Chagas's disease. This test is positive only in that disease with the exception that weak reactions are given in cutaneous leishmaniasis. The authors give details of their results.

HAUSCHKA *et al.* (p. 1054) have shown that infection with *T. cruzi* significantly retards the growth of certain tumours in mice.

EARLE (p. 53) reports a case of Chagas's disease which cleared up, apparently as a result of intravenous administration of penicillin.

Charles Wilcocks

## RABIES

REMLINGER, P & BAILLY, J La rage Etudes cliniques, expérimentales et immunologiques [Rabies Clinical, Experimental and Immunological Studies] pp v+192 [Bibliography] 1947 Paris Librairie Maloine, 27 rue de l'École-de-Médecine [18s 6d]

The volume under review summarizes 320 studies on rabies made between 1903 and 1946 by Remlinger and his collaborators. Of these studies, 169 are by Remlinger, 4 by Bailly, 135 conjointly, and 12 by one or other of the authors assisted by LEGER, TEPPAZ, BEL, CURASSON or MICHEL.

Although it is in no sense a textbook on rabies, nevertheless, thanks to the authors' admirable arrangement of the subject matter and to their clear and concise treatment of a majority of the problems likely to face workers in this field, the volume will form a welcome and valuable addition to the reference libraries of anti-rabies institutes.

While it is true that most of the information now presented in so attractive and readable a form will be familiar to the specialist in rabies and its treatment, yet certain of the authors' conclusions and opinions merit special attention and justify recapitulation.

#### *Rabies virus*

*Street v Fixed Virus*—The "singleness" of street virus is contrasted with the "plurality" of fixed virus—a virus "fixed" only in name. Proof of "singleness" is afforded by cross-immunity experiments with variously derived street virus strains, including those endowed with hypernormal virulence ("renforcés"). Proof of "plurality" of fixed virus is based on the wide variation, ranging from the exclusively paralytic to the purely encephalitic, in the symptomatology of rabies among rabbits used in treatment, particularly as regards the day of death, and on the difference in the resistance of such viruses to attenuating agents and in their pathogenic power for the anterior chamber of the rabbit's eye and for the cellular tissues of man and dog.

*The nature of rabies virus*—The hypothesis first advanced by Remlinger in 1918 that rabies is due to a chemical substance of a protein nature, on the frontier between the organic and the inorganic, receives support, by analogy, from the work carried out in 1935 by STANLEY and his colleagues on the virus of the mosaic disease of plants. STANLEY was able to crystallize the latter virus, discovering it to be a macromolecule of protein, reproducing itself apparently by a process of autocatalysis. Such a conception, if somewhat at variance with the more popular microsporidial theory of rabies virus (*Glugea lyssae*, *Encephalitozoon rabiei*), is not wholly irreconcilable therewith.

*Anti-rabies treatment*—The "singleness" of street virus obviates the need for polyvalent or autogenous vaccines, failures of treatment, even in the case of reinforced viruses, are attributable almost entirely to insufficient therapy. Standardization of treatment is a desideratum, to be achieved possibly by providing all anti-rabies institutes with the same strain of fixed virus, one combining a high degree of immunizing power with complete innocuity. Were such standardization to prove acceptable, phenolized killed virus vaccine would bid fair to becoming the product of choice, by virtue of its undoubted efficacy, its keeping properties, the decentralization which its use makes possible and its comparative freedom from neuroparalytic accidents.

A strong plea, founded on the experience of French North African territories, is made not only for canine prophylaxis but also for the treatment of dogs and other domestic animals bitten by rabid animals. For canine prophylaxis, use is made of a 5 per cent fixed virus rabbit-or dog-brain, in 1 per cent phenolized water, inactivated at 37°C, of this vaccine 40 cc are administered on the first

day 24 hours afterwards a further dose of 40 cc. is given. Revaccination annually with 40 cc. is advocated. In the treatment of dogs bitten by rabid animals 3 to 10 injections, each of 40 cc. of the same vaccine, have been followed by encouraging results. Similarly in the case of horses and cattle success has attended the exhibition of 40 cc. of the phenolized vaccine on 3 successive days in severe head bites a further dosage of 40 cc. is administered on the 4th day a total of 120-160 cc. is advised according to gravity of wounding.

Finally the need for an international rabies conference, similar to that held in Paris in 1927 is urged. Items on the provisional agenda suggested include the nature of rabies virus the influence of rabbit passage on the susceptibility of fixed virus to the action of attenuating agents the possibility and desirability of standardization of treatment the neuro-paralytic accidents of treatment the vaccination of dogs before and after having been bitten and the vaccination of domestic animals generally.

G. Smart

## MALARIA

I. SHORRIT H. E. & GARNHAM P. C. C. Pre-erythrocytic Stage in Mammalian Malaria Parasites. [Correspondence.] *Nature*, 1948, Jan. 4 128.

II. ——— & MALANOS, B. The Pre-erythrocytic Stage of Mammalian Malaria. *Brit. Med. J.* 1948, Jan. 31 162-4 4 figs. [14 refs.]

III. HAWKING F. Pre-erythrocytic Stage in Mammalian Malaria Parasites. [Correspondence.] *Nature*, 1948, Jan. 31 175.

I & II. Attempts to discover the developmental forms of sporozoites of *Plasmodium cynomolgi* in the monkey by the Mammalian Malaria Enquiry (this Bulletin 1947 v 44 966) working in India, by HURT and COULSTON in America [ibid 1945 v 42 536] and by others have yielded only negative results. The authors of the present notes have been more fortunate, as they have discovered the pre-erythrocytic stages in two monkeys receiving large doses of sporozoites. Of a batch of *Anopheles maculipennis atroparvus* fed ten days before on an infected monkey dissection of 20 showed that all were heavily infected. Accordingly 578 mosquitoes were given the opportunity of feeding on a clean rhesus monkey. Over 500 of the mosquitoes fed. The mosquitoes were then ground in a mortar in 10 cc. of heparinized monkey plasma diluted with normal saline solution. Half the suspension was inoculated intraperitoneally and the other half into the thigh muscles of the same monkey. The suspension showed an average of 5 sporozoites per field of the 1/12" objective.

The monkey was sacrificed seven days later and a complete examination was made. Though all the tissues have not been thoroughly examined, inspection of the liver sections and smears has revealed what is undoubtedly the pre-erythrocytic developmental forms in the shape of multinucleated plasmodial masses measuring 20 to 30µ in longest diameter and containing 200-300 nuclei. In a number of the schizonts are one or more vacuoles. The extent of infection of the liver is shown by the occurrence of 30 schizonts in a section measuring 90 sq mm.

Suspensions of liver spleen, brain lung kidney, peritoneal fluid and heart blood were inoculated to clean monkeys which had remained negative for one month at the time of writing. Similar bodies were found in the liver of a second monkey killed on the 6th day after mosquito feeding and injection of sporozoites. In this case the schizonts were smaller and it was possible to determine that the parasites were in the parenchyma cells.

The importance of this discovery lies in the fact that *P. cynomolgi* resembles *P. vivax* of man very closely, this strengthens the belief that such forms are likely to occur in human malaria.

iii. Hawking, who has been studying the early development of *P. cynomolgi* for some time without success, was shown the preparations of SHORTT, GARNHAM and MALAMOS and returned to his own preparations. In livers of three monkeys which had received sporozoites of *P. cynomolgi* he discovered similar pre-erythrocytic schizonts. One rhesus monkey had been inoculated intravenously and parenterally with the sporozoites from 120 infected mosquitoes. It was killed 7 days, 23 hours later. Large schizonts,  $28\mu$  in diameter, were found in the liver, similar forms were found in the liver of a monkey killed 7 days 15 hours after intravenous injection of the ground-up thoraces of 1,000 infected mosquitoes. A third monkey inoculated intravenously with the suspension of 40 infected mosquitoes was killed 5 days later. Schizonts  $14\mu$  in diameter were found in the parenchymatous cells of the liver. Inoculation of emulsion of organs of these monkeys was not followed by infection. C. M. Wenyon

BULL. WORLD HEALTH ORGANIZATION (United Nations) 1947/48, v 1, No 1, 21-8. **Expert Committee on Malaria**. Extract from the Report on the First Session, Geneva, Palais des Nations, 22-25 April 1947.

The urgent importance of the malaria problem caused the Committee on Epidemiology and Quarantine of the Interim Commission of the W.H.O. to set up an Expert Committee to examine it. This Expert Committee met in Geneva in April 1947, and submitted its report, of which this paper is an extract, in August of the same year.

The Expert Committee formed a natural link with the former Malaria Commission of the League of Nations but a very different field of work confronted it, for the intervening years had brought about new problems and new solutions, and, indeed, the very conception of the mechanism of malarial infection had itself changed, with the newer discoveries regarding the exoerythrocytic cycle.

The original Report comprises ten sections, a number of which are concerned with administrative questions. The extract under review deals more specifically with certain technical aspects of the problem, notably those relating to suppressive treatment, causal prophylaxis, new synthetic drugs and new means of administration of former ones, and the development of new contact insecticides. All of these subjects have been dealt with fully in this *Bulletin* during recent years. The present paper refers briefly to the successes achieved during and since the recent war in the chemotherapeutic control of malaria and its epidemiological control by means of DDT.

Reference is made to the successful field experiments with atabrin [mepacrine], to the work on the 4-amino-quinolines, sontochin (SN 6911) and chloroquine (SN 7618), the 8-amino-quinolines, such as pentaquine, and the biguanides, of which the most important is paludrine.

The use of DDT as a larvicide and more particularly as a mosquitocide is briefly reviewed. The limitations of its use in the former capacity are noted, and it is pointed out that DDT, especially when used from aeroplanes, may upset the economy and normal biological cycles of a region, from the standpoint of animals, crops and trees.

The value of DDT in destroying the adult vector of malaria is supplemented by its effect on other domestic insects, and it may thus influence indirectly the local morbidity from causes other than malaria.

Large-scale house-spraying with DDT will depend on the budgeting facilities of each country concerned, the Report discusses the economic aspects of this matter and the Committee emphasizes that the time has come when more

effort should be devoted to developing methods for more practical and economical control of malaria with this powerful weapon. It is pointed out that, to maintain a reduced incidence of diseases after successful control by DDT the latter will probably have to be used as a recurring measure, and this will require to be taken into account when over-optimistic health authorities are contemplating a budgetary reduction. *H J O'D Burke-Gaffney*

SPADARO O Indice splenico ed indice parasitario in gruppi di popolazione araba in arrivo nel porto di Massawa. [Spleenic and Parasitic Indices in a Group of Arab Immigrants in Massawa.] *Boll. Soc. Ital. di Med. e Ig. Trop* (Ser. Entrec.) 1947 v 7 No. 3/4 259-61

The English summary appended to the paper is as follows —

The author has searched the spleen index and the parasite index in a group of natives of the Northern Dankalia and of the Yemen who came to Massawa for work. Both groups have given a comparatively low index.

MAUZÉ, J Contribution à l'étude du paludisme dans les Nouvelles-Hébrides (particulièrement pendant la campagne du Sud-Ouest Pacifique Janvier 1942-Décembre 1943). [Contribution to the Study of Malaria in the New Hebrides, chiefly during the War in the South-West Pacific, January 1942 to December 1943.] *Méd Trop Marseille* 1946 v 6 No. 2, 109-33 7 graphs & 1 pl.

There are very scant references in the literature to malaria in the New Hebrides. In collecting material for this report the author expresses indebtedness to assistance given by colleagues of the United States Forces during their stay in this island group.

The New Hebrides archipelago lies between New Caledonia, in the south, and the Solomon Islands, and about midway between Fiji and the east coast of Queensland. More than 40 of the islands are inhabited some of these are very small, 120 to 1,200 acres, or even less. The largest island, Espiritu-Santo covers an area of 5 000 square kilometres. The second largest, Malakula is about half that size. The islands are of both volcanic and coral formation volcanic activity is manifest in many of the islands. The kanaka population probably does not exceed 50 000 no census has ever been taken. In addition there are 909 French English and half-castes, most of whom live in Vale, the capital in the island of Vati.

The New Hebrides have always had an evil reputation for malaria. Hospital and dispensary attendances during three recent years show it to be the most prevalent disease malaria 4,267 pulmonary diseases 2,531 yaws 942, amoebiasis 895 syphilis 502, gonorrhoea 457 and helminthiasis 206. Seven weeks after the installation of a contingent of United States marines in the island of Vati, 47 per cent. of its strength were incapacitated by malaria.

*P. falciparum* is the most prevalent parasite, about 75 per cent. of all infections; *P. malariae* about 15 per cent. and *P. vivax* about 10 per cent. Serious clinical forms of malaria are relatively rare.

The only *Anopheles* found in the New Hebrides is *A. punctulatus* or *malaccensis* (now known as *A. punctulatus farauti*) of which detailed morphological and biological descriptions are given. It is ubiquitous. It has a great variety of breeding places in the dry season larvae are found in rivers streams, springs, irrigated land, seepages and open wells, and in the rainy season in many collections of casual water as well. The water may be clear turbid stagnant, saline or almost pure rain water and with or without vegetation. The only



waters in which larvae have not been found are open surfaces of running water, and water in broken coconut shells and holes in tree trunks

The New Hebrides mark the southernmost extension of anophelines and malaria in the Pacific in New Caledonia there are neither

Norman White

PENIDO, H M Alguns aspectos da epidemiologia e controle da malaria na area do Rio Doce [Certain Aspects of the Epidemiology and Control of Malaria in the River Doce Area] *Rev Serviço Especial de Saude Publica* Rio de Janeiro 1947, v 1, No 1, 61-76, 1 map & 1 chart English summary

In this contribution to the first inter-American Congress of Medicine, the author outlines the malaria problems and malaria control measures applied in 33 townships situated along 660 kilometres of the Vitória-Minas Railway. From Vitória, a coastal town in the State of Espírito Santo, the railway runs north 950 kilometres to reach the River Doce near Barbados. There it turns westward and enters the State of Minas Gerais, it runs alongside the River Doce to Ipatinga (458 km). From Ipatinga it runs along the valley of the Piracicaba River, a tributary of the Doce, to Dezenbargador Drummond.

The intensity of malaria varies considerably in places along the track from Vitória to Barbados in Espírito Santo. A random sampling of the blood of persons living in 12 places in May of each of four years showed Alfredo Maia to be the most heavily infected, the percentage of positive slides varying from 11 to 30.8. Along the whole railway, *A. darlingi* is the most important vector, the only one except in the first hundred kilometres from Vitória where *A. albicans* is also very prevalent. In the neighbourhood of Vitória, *A. aquasalis* also transmits malaria. The oöcyst rate of 781 *A. darlingi* dissected was 7.5 and of 226 *A. albicans* 1.3 per cent. The examination of patients attending medical posts along the first 150 miles of track showed that *P. vivax* infections were more numerous than *P. falciparum* infections, except in March and April, the end of the rainy season. *P. malariae* infections were rare.

The first two hundred kilometres of the line up the Doce Valley are practically free from malaria, the river bed is narrow and confined, but from Derribadilha to Dezenbargador Drummond, 210 km, settlements on the banks of the Doce and Piracicaba Rivers are intensely malarious. Positive findings in samples of blood films taken in the month of May in four consecutive years in 21 localities show the intensity of infection, in one case the infection rate was 50 per cent. Dispensary records show that in this part of the line also, *P. vivax* exceed *P. falciparum* infections in number except in the rainy months February to May. In April *P. falciparum* infections were more than double those of *P. vivax*.

The rainy season begins at the end of October or early November and 1,500 mm of rain fall in five or six months. The river overflows its banks and actual and potential breeding places for *A. darlingi* are enormously increased. Antilarval control becomes almost impossible, epidemic malaria ensues, its severity being determined by the nature of the rainfall. In the dry season, however, antilarval measures have been carried out with success, chief reliance has been placed on Paris green and small drainage work. The method of work is described.

DDT promises to provide a much more economical method of malaria control in areas that have as low a density of population as has the Doce Valley. A start has been made. An aqueous suspension of DDT has been applied at the rate of 2 gm per square metre. It is proposed to treat the houses three times a year. [For details of control measures used, see BRAGA *et al.* below p 408.]

Norman White

SCHWETZ, J. Sur la anophélie et le paludisme endémique et épidémique des noirs dans les régions de hautes altitudes de l'Afrique intertropicale. [The *Anopheles* and the Endemic and Epidemic Malaria of Africans in Elevated Regions of Tropical Africa.] *Rev de Malariologie*. 1947 Oct. v 28 No. 5 227-33.

This paper is a concise summary of the results of numerous investigations carried out by the author in the Belgian Congo. All the facts have been described in previous publications and have been duly noted in this *Bulletin*. Chief consideration is given to the *Anopheles* and malaria at high altitudes along the eastern frontier of the Belgian Congo [this *Bulletin* 1947 v 41 789].  
Norman White

WOLFE, J. Sur la faune culicidienne de l'agglomération de Coquilhatville. (Troisième note.) [The Mosquitoes in the Coquilhatville Region.] *Ann. Soc. Belge de Méd. Trop.* 1947 June 30 v 27 No. 2, 263-71 1 fig. & 1 chart on pl.

In 1946 the author continued investigations which he had made previously into the breeding places of *Anopheles mouchelet* along the banks of the river Congo but had no success because of the backwash caused by the boats which continually pass up and down the river. In backwaters along the Ruki river the water was too foul to admit of breeding by this mosquito and so he comes to the conclusion that most of the *A. mouchelet* that infest Coquilhatville come from the islands in the river (Congo).

Brief notes on the breeding places of species of *Aedes* are given and there is a list of 6 species of anophelines and 44 culicines recorded in 1944 and 1945 which shows that the common species are present all the year round.

H. S. Lensen

WANDON, M., WOLFE, J. & LERIED, B. Comportement de l'*Anopheles (Mysomyia) mouchelet* EVANS. [The Bionomics of *Anopheles mouchelet*.] *Rev. Trav. Sci. Méd. Congo Belge*. 1947 July No. 6 30-62 2 charts. [25 refs.]

This account of the bionomics of *Anopheles mouchelet* is the result of observations made at Coquilhatville and at Léopoldville in the Belgian Congo. Data are given and compared with those obtained by other workers at Stanleyville and Yangambi and, where relevant with those for *A. gambiae* because though this anopheline is more common in some places at certain times, it is not so common as *A. mouchelet* at Coquilhatville. Matters discussed include numerical abundance and seasonal prevalence, types of breeding places and larval requirements, the influence of distance between breeding and feeding places, outdoor and indoor resting places, longevity and feeding habits of the females and their infectivity with the plasmodium of malaria.

For breeding, this mosquito requires fresh water constantly replenished and shaded—these conditions it finds on the alluvial islands in the river (Congo) and even when the water rises at flood time larvae may be found among dense masses of reeds at the downstream ends of the islands where they are sheltered from the current. Larvae are also to be found among floating vegetation which has broken away from the islands and the river banks. At Léopoldville (Stanley Pool) the islands are not so numerous and the height of the water reduces the number of breeding places, thus limiting the output of adults. In mid-November about three weeks after the floods have reached their maximum breeding places are again available and in January the mosquito catches in the prison which is the nearest catching station to the Pool, yield three times as many *A. mouchelet* as *A. gambiae*.

Outside haunts of this anopheline at Coquilhatville are found among trees, in the shade and not far from the breeding places, but they have not yet been discovered at Léopoldville. A study of the feeding habits and the ovarian development of females has shown that the majority found in houses possess ovaries in stages I and II. Typical figures for outdoor catches give 20 per cent females with ovaries in stage V and 60 per cent for females which have not fed. In fishermen's huts on the islands, examination of 500 females of *A. mouchei* showed 31 per cent with stage V ovaries and only 3 per cent in stage I. Sporozoite rate at Coquilhatville is 0.072 per cent, whereas at the fishermen's huts at Stanley Pool the rate is 6.3 per cent.

From these observations and a great many more, the authors conclude that, *A. mouchei* is short-lived; that the female needs only one blood meal to mature the eggs, that it enters houses, rests for some time before feeding and then leaves immediately to digest the meal and to mature the eggs outside; there is evidence also that the sporozoite index is fairly constant in any one locality, and varies only according to the distance from the breeding places.

In the laboratory, *A. mouchei* has been observed to deposit an average of 200 eggs per female; eggs hatch in 12 to 24 hours and the larval stage lasts 10 to 11 days. The whole life cycle can be completed in 13 to 14 days and males and females emerge in approximately equal numbers. The authors have not yet succeeded in establishing a laboratory colony. The discovery of a blue coloration infiltrating the thoracic muscles is a matter for future investigation.

H S Leeson

LAUTERBURG-BONJOUR, M. Die Abwehrfunktionen des menschlichen Körpers gegen die Malaria. [Defensive Functions of the Human Body against Malaria.] *Schweiz med Woch* 1947, Dec 27, v 77 No 52, 1359-62

In his discussion of immunity in malaria, the author concludes that it is not a simple process but is very complex. Apart from normal phagocytosis there is a phagocytosis which is stimulated by parasitic and antitoxic substances which have been demonstrated in the blood. The immunity is strongly specific, not only for the kind of malaria but for the particular race of parasite. In endemic areas a latent malarial infection is of value in that it prevents reinfection with the same race of parasite. Such a latent infection in persons going to new malarial localities is not able to prevent infection with any new race to which there is exposure.

C M Wenyon

BOYD, M F & KITCHEN, S F. On the Homogeneity or Heterogeneity of *Plasmodium vivax* Infections acquired in highly Endemic Regions. *Amer J Trop Med* 1948, Jan, v 28, No 1, 29-34

It was noticed that some soldiers returning to the USA from highly endemic areas in the Pacific, developed repeated attacks of *P. vivax* malaria. The intervals between these attacks were usually short, and the febrile episodes were thought to be recrudescences rather than relapses (as defined by Boyd & Kitchen, this *Bulletin*, 1945, v 42, 174). The men had been on daily suppressive quinaquine and the malaria did not appear until this therapy was discontinued. The authors considered that several strains of *P. vivax* were acquired and either that all these strains were reactivated simultaneously during the recrudescences or that some strains would recover from the "quinaquine induced lethargy" earlier than the remainder. If the first explanation were correct, the parasites of the various recrudescences should show complete cross immunity. On the other hand, if each recrudescence represented an infection by heterologous strains, then cross immunity should be lacking.

Mental patients were therefore hyper immunized against one of three strains recovered from a young soldier who had suffered from many attacks of *P. vivax* malaria contracted in the Pacific. The results indicated that two of the strains appeared to be closely allied if not identical while the third showed a substantial difference.

P C C Gernham

MAKARI J G Intradermal Test in Malaria. Parts I, II & III. *J Trop Med. & Hyg.* 1948, Apr-May & June-July v 49 Nos. 2 & 3 23-9 47-54 7 figs. [19 refs.]

The antigen for this test was obtained from the blood of a chicken heavily infected with *P. gallinaceum*. Heart blood was put in small oxalated tubes, 2 cc. in each. Plasma was separated by centrifuge and discarded. The corpuscles were washed four times with saline and then dried *in vacuo*. After 2 months they were transferred to clean test tubes and sealed, and kept at room temperature, about 30°C. for two months. To prepare the stock solution the powder was triturated in a mortar. A suspension of 1 per cent. of this powder in 0.5 per cent. carbollised salt solution was then prepared, and incubated for 24 hours at 37°C. It was then passed through a Seitz filter and tested for sterility. This sterile fluid was used in the intradermal tests.

In making the test 0.1 ml. was injected intradermally on the forearm. Readings were taken after 24 hours. The diameter of redness was measured in millimetres and the results were recorded as follows:

0-4 mm.	0
5-9 mm.	+
10-14 mm.	++
15-19 mm.	+++
20 mm. and over	++++

Of 70 persons with no history of malaria, 63 gave a negative reaction, 5 had a + and 1 had a ++ reaction.

Of 71 patients who had had malaria 18 months previously 65 gave a positive intradermal test.

Of 31 others having a history of malaria within 3 years or more, 29 gave a positive test.

The sensitivity of the tissues to the malarial antigen appears to reach its peak from 2 to 3 months after an attack. In the majority of cases it is never lost completely.

II. Another antigen N was prepared from normal chicken erythrocytes in the same manner as was the malarial antigen M from malaria-infected erythrocytes described above. Antigen N gave positive reactions in 14 per cent. antigen M in 20 per cent. of 70 boys with no history of malaria. These pseudo-positive reactions were all weak (+). Of the false reactions to antigen N 90 per cent. were in individuals of blood groups O or B in both cases having anti-A antibodies which would react with the A like Forssman antigen found in normal chicken red cells. Antigen N gave weak positive reactions in 40 per cent. of the malarial series. Malarial infection stimulates the production of heterophile antibodies. The control testing with normal antigen N should always accompany the testing with malarial antigen M to eliminate a number of false positive reactions.

III. The author believes that a combined use of the intradermal test and the cephalin cholesterol flocculation test [this *Bullet.* 1948, 43, 623 1947 v 44 279] would assist in the detection of chronic, masked and latent forms of malaria and the determination of the activity of the infection in assessing the rôle of malaria in determining false positive serological reactions.

in ruling out malaria in the blood plasma programmes , and in solving problems created by returning malaria carriers from overseas *Norman White*

**MAKARI, J G** Altered Tuberculin Sensitivity in Chronic Malaria *J Trop Med & Hyg* 1947, Sept, v 50, No 9, 183-5 [11 refs]

The author has submitted a number of Armenian refugees, in Syria, to the tuberculin test, the intradermal malaria test [see above], and the cephalin-cholesterol flocculation test. There were 58 persons with chronic malaria, and 60 in whom malaria was excluded by negative history and negative intradermal test.

In general, the results indicated that the incidence of positive tuberculin tests (OT, 1 in 1,000) was higher (41.4 per cent) in those with chronic malaria than in the controls (23.3 per cent) and that the difference is statistically significant. Moreover, the incidence of positive tuberculin tests appeared to be related to the activity of the malaria, as estimated by the cephalin-cholesterol test, and to the sensitivity of the tissues in response to the malarial antigen.

The author discusses the possibility that there may be a relationship between the proteins of the tubercle bacillus and the malaria parasite, that the tubercle bacillus may have a predilection for tissues damaged by malaria, and that persons with chronic infections may react more readily than normal persons to antigens other than those from the organism infecting them.

[The author places a high degree of reliance on the cephalin test, but in a previous paper (this *Bulletin*, 1946, v 43, 623, 1947, v 44, 279) he claimed accuracy of only 91.4 per cent for it. It seems likely that the cumulative errors of all these tests might be considerable.] *Charles Wilcocks*

**SCHEIFLEY, C H** Malaria a Note on its Latency and Report of a Case *Proc Staff Meetings Mayo Clinic* 1947, Feb 5, v 22, No 3, 49-52

"It is commonly thought that a primary attack of malaria may occur a year or more after cessation of suppressive medication. A review of the literature failed to reveal any well-documented reports to bear out this assumption. In the case reported in this paper, benign tertian malaria developed twelve months or more after suppressive therapy had been discontinued."

**BOYD, M F** A Note on the Chronicity of a Quartan Malaria Infection *Liber Jubilaris J Rodham (Soc Belge Méd Trop, Brussels)* 1947, Dec, 99-101

"A naturally induced *P. malariae* infection has persisted in a latent chronic condition in a colored patient for a period of 4,305 days, or 11 years, 9 months, 14 days since the original inoculation."

**SOYSA, E** Malarial Episodes A Clinical Study of Atypical, Pernicious and Lethal Cases selected from among 10,000 Malarial Patients admitted to Military Hospitals in Ceylon *J Roy Army Med Corps* 1947, Nov, v 89, No 5, 205-22, 3 figs

To illustrate the diversity of clinical features that may result from malarial infections the author has selected twelve cases from the 10,000 that were treated in two military hospitals in Ceylon during a period of four years. All the cases present unusual features and are fully and well described. They illustrate apyrexial malaria, hyperpyrexia, algid malaria, cerebral malaria, malaria encephalopathy, malarial neuritis, malarial jaundice, malarial dysentery,

severe malarial anaemia, malarial leucopenia, malarial haemoglobinuria and malarial pneumonia. The nature and length of this interesting paper preclude a summary  
Norman White

MELLINKOFF S. M. & HIGGINS J. R. The Heart Rate in Malaria; a Review of Ninety Cases. *Ann. Intern. Med.* 1947 Sept. v 27 No. 3 433-40 4 figs. [10 refs.]

This paper concerns the heart rate in 90 patients suffering from malaria contracted for the most part in the Philippine Islands. In most cases, the appearance of clinical symptoms had been delayed by the administration of prophylactic doses of atabrin. There were 85 patients with *P. vivax* infections, 2 with *P. falciparum* and 3 with *P. malariae*. The pulse readings record the greatest relative tachycardia observed at the height of each initial fever. After the subsidence of fever and malaise the resting pulse rate was recorded in each case, an hour after the patient had awakened from a good night's sleep, the interval hour having been spent in bed. The results of the study show that malarial fevers may be accompanied by rates of heart beat ranging from tachycardia like that which characterizes many bacterial infections to bradycardia like that of typhoid fever. About one-fourth of these patients had relative bradycardia.  
Norman White

BOWERS, B. Neuropsychiatric Manifestations during the Course of Malaria. Experiences in the Mediterranean Theater in World War II. *Arch. Neurol. & Psychiatry* 1947 July v 58 No. 1 14-23 2 figs. [Refs. in footnotes.]

The author deals with his experiences in the Mediterranean war area, where malaria was a common disease among American armed forces with special reference to the neuropsychiatric complications of malaria that were encountered. These complications simulated meningitis, encephalitis, cerebral tumour, vascular lesions and psychiatric disorders. Such cerebral forms of malaria were not exclusively caused by *P. falciparum* infections. *P. vivax* was sometimes incriminated. The clinical history of an illustrative case is described.

A man aged 26 fell ill with a chill and slight fever. Two examinations of the blood were made but no parasites were found. Symptoms of meningo-encephalitis developed rapidly with characteristic changes in the spinal fluid, the suspicion of a virus infection was not confirmed. Convulsions developed and the diagnosis of epilepsy was considered but the presence of coma, a temperature of 102.30 F. and meningeal symptoms negatived this. Then followed an afebrile period of several days during which the cerebrospinal fluid became normal, but evidence of transient focal disturbances in the brain remained. Still no malaria parasites were to be found. On the 8th day a generalized convulsion occurred, followed by a Jacksonian fit on the right side, sodium amytal aborted a threatened status epilepticus. Four days later a right homonymous hemianopia was detected, and persisted. On the 19th day of illness the temperature rose to 101.8° and *P. vivax* was found in the blood. Quinine was administered. All the symptoms cleared up quickly except the hemianopia. The case was undoubtedly one of malarial meningo-encephalitis with multiple neuropsychiatric manifestations. Norman White

ANDREWS J. C. & CORMATZER, W. E. The Metabolism of Cinchonine in Dogs and in Man. *J. National Malaria Soc.* 1947 Dec. v 8, No. 4 248-50. [10 refs.]

The authors showed previously that cinchonine was absorbed more rapidly than quinine from the isolated intestinal loops of dogs. BLATT [this Bulletin

1945, v 42, 178] on the other hand, found that only low concentrations of the former were present in human plasma after oral administration compared with those of the other common cinchona alkaloids, indicating a possible difference in the rate of absorption of the two optical isomers cinchonine and cinchonidine. When the four alkaloids were given intravenously to man, HATT & QUINN [this *Bulletin*, 1945, v 42, 778] found that their distribution in the body was similar. It is possible therefore that the rate of metabolic breakdown varies in the case of these different alkaloids. Data were therefore obtained on the blood levels and urinary excretion of cinchonine in man and dog by means of the intestinal loop method of the authors [this *Bulletin*, 1945, v 42, 534] in the animal experiments. The results indicated that cinchonine is metabolized more rapidly than cinchonidine or quinine in man. In the dog the rate of metabolic breakdown appeared to be much slower. The results are of interest, since some authors believe that the antimalarial effect of cinchona alkaloids is due to a metabolic product of those substances.

J D Fulton

CHEN, G. Influence of Pamaquine and Atabrine on the Enzymatic Degradation of Quinine. *Proc Soc Exper Biol & Med* 1947, Nov, v 66, No 2, 313-14, 3 figs

KELSEY & OLDHAM [this *Bulletin* 1944, v 41, 260] found that, of various animal tissues, rabbit liver was richest in the enzyme, termed by them quinine oxidase, which converted the alkaloid to the substance which MEAD & KOEFFLY [ibid., 1945, v 42, 9] characterized as a 2-hydroxy derivative. A method has now been developed for the quantitative assay of this enzyme, and its inhibition by plasmoquine (pamaquin) and atabrin (mepacrine) have been investigated. For this purpose, fresh rabbit liver was homogenized in Ringer-Locke solution. On centrifuging, all the enzymic activity was found to be present in the supernatant fluid. The latter was therefore used in all the experiments, in which quinine in Ringer-Locke solution and the enzyme were incubated at 39°C for appropriate times. Enzyme action was then inhibited by the addition of an equal volume of 4 per cent caustic soda. The unchanged quinine was estimated by the fluorometric method of CHEN & GEILING [ibid., 1945, v 42, 348] in a Coleman photofluorometer, with the use of suitable filters when plasmoquine and atabrin were present. The relationship between the percentage degradation of quinine and the logarithm of liver concentration used was linear except in the early stages of the reaction and a roughly similar relationship held when the former values were plotted against the logarithm of reaction time. By choosing a reaction time of one hour, the graphs allowed the activity of an enzyme preparation to be determined. Both plasmoquine and atabrin inhibited the conversion of quinine. While the mode of action of these substances is not quite clear, it is believed that they act on the enzyme rather than on the substrate.

J D Fulton

DEARBORN, E H. The Distribution of Quinacrine in Dogs and in Rabbits. *J Pharm & Exper Therap* 1947, Oct, v 91, No 2, 174-7

"The concentration of quinacrine in the plasma of rabbits and dogs shows marked variation. There is no significant correlation between the concentration of quinacrine in the plasma and that in the tissues of rabbits and dogs. The concentration of quinacrine in muscle and its ratio to the concentration in the plasma tend to increase in dogs on a constant daily dosage."

TRACER, W. The Rate of Asymptomatic Malarial Infection in White and Negro Service Troops taking Suppressive Atabrine. *Amer J Hyg* 1947 Nov v 46 No 3 338-40

The author in collaboration with HAWC and others, has previously shown that malarial parasites may sometimes be found in thick blood films from men taking adequate suppressive doses of mepacrine and having no clinical symptoms of malaria [this *Bulletin* 1947 v 44 503]. In Finchhafen New Guinea, he made a study of three pairs of Army units, one unit of each pair consisting of whites, the other of negroes. The units of each pair were living under strictly comparable conditions as regards the risk of malaria infection. The men were all taking, or supposed to be taking, 0.1 gm. of mepacrine a day. The results of the study during the 4 to 8 weeks period of observation were as follows—

	Unit					
	A	B	C	D	E	F
Race	White	Negro	White	Negro	White	Negro
Men studied	87	82	93	85	108	102
Average smears per man	5.2	5.5	3.8	2.8	2.7	2.8
No. with one positive smear ..	18	11	20	9	20	17
No. with two positive smears	3	2	3	1	2	1
Per cent. with parasites	23	15	24	12	22	17
No. from south-eastern U.S.	0	4	27	1	15	89
No. who had had clinical malaria in U.S.A.	0	0	2	0	3	19
No. who had had clinical malaria in New Guinea	0	0	1	1	0	1

Most of the parasites found were ring forms. A few old trophozoites were seen, but only one gametocyte (*P. vivax*). It is probable that all the parasites were *P. vivax*. Only one man had three positive smears (Unit E) he had parasite counts of 132 and 55 parasites per 500 white cells in three successive weeks, but had no symptoms of malaria. Very few of the other positive smears contained more than 4 parasites per 500 white cells. The author has previously shown that the finding of these occasional parasites bears no relation to the mepacrine blood level.

Norman White

PARK, D. Mepacrine Psychosis. *J Mental Sci* 1947 Oct. v 83, No. 293 756-71 [12 refs.]

Not all cases of psychosis in patients with malaria treated with mepacrine are necessarily true cases of mepacrine psychosis. It is possible that the symptoms began before the exhibition of mepacrine and were precipitated either by malaria or by circumstances antecedent to it or the condition was present before mepacrine therapy and was aggravated by the drug. In true mepacrine psychoses, the symptoms are precipitated by the administration of mepacrine. Twenty three cases of true mepacrine psychosis seen in the Middle East are described: all were males and British except for two Palestinian Jews. The proportion of officers and N.C.O. to privates was as 11 to 1 and is said to be high compared with the ratio in the command; the ratio is not given. The most common mental make-up of the patients was schizoid, 6 cases. The aetiology of mepacrine-precipitated cases is thought to be multifactorial and in addition to malaria, emotional stress may have contributed in 7 cases, recent battle stress in 3 and alcoholism in 2 cases. Eleven patients had had one or more attacks of malaria in the 18 months before the psychiatric episode. Three



patients gave histories of previous psychotic breakdowns and in one other psychotic symptoms appeared during a subsequent attack of malaria when quinine and pamaquin were given. Of the 23 patients, only one had been on suppressive mepacrine—he had taken 0.2 gm for 9 months, and the breaking-off of his engagement is said to have precipitated the attack.

The psychotic symptoms appeared when the standard treatment for malaria was 3.4 gm of mepacrine in 6 days. One-third of those affected developed mepacrine psychosis on the third or fourth day of treatment, the remainder usually within 7 days of the end of treatment. In one case, symptoms began in less than three days and in another (included as having been precipitated by mepacrine) not till 3 months after the cessation of mepacrine therapy [on the dose schedule given, it is very doubtful whether more than minimal traces of mepacrine would have been found in the body after this interval].

There was no significant difference in the time of recovery between those developing the psychosis early and those who developed it late.

The most frequent symptoms were schizophrenic and manic in type. Malaria, on the other hand, more commonly produces a depressive reaction. The onset is almost invariably signalized by insomnia and in the non-depressive cases by a sudden change of behaviour, with noisy talkative excitement. The psychotic picture then develops rapidly—there is a brief phase for a day or two of features such as fleeting ideas of influence, loss of personality and reality sense and sometimes transient confusion and disorientation. This is followed by elation, euphoria and delusions of an exalted character. Eight typical case histories are recorded.

Fourteen of the 23 patients recovered within 6 months of the onset of symptoms, the quickest being in 14 days, the average 62 days. Those with manic and schizophrenic symptoms recovered most quickly. Mepacrine psychoses occur more frequently in a slightly older age-group than do those due to malaria. Electrical convulsive treatment was used in six cases. 4 of these (two with schizophrenia and two with depression) improved but 2 remained unchanged. The number of convulsions ranged from 2 to 6, averaging 4.6.

Diagnosis requires differentiation from cerebral malaria and from an endogenous or biogenic psychosis.

It is stated that the medical attendant should be on his guard in exhibiting mepacrine to those who have had recent attacks of malaria, show evidence of hepatic derangements, have taken suppressive mepacrine in large doses or suffer from any factors which delay the excretion of mepacrine.

The danger signals which are said to call for the stoppage of mepacrine in the treatment of a malarial attack are staining of the skin and the occurrence of insomnia, alteration of conduct, restlessness, talkativeness and confusion.

[Few will agree with the contention that staining of the skin necessitates cessation of mepacrine therapy. Those in army commands serving in hyper-endemic malarial areas were almost all tinted yellow by mepacrine—eccentric some of them may have been—but they were not on the verge of a mepacrine psychosis.]

G M Findlay

BUONOMINI, G & MOTTA-DIANA, A. Trattamento abbreviato con acridinici dell'attacco malarico sua utilità nella pratica dispensariale [Short Treatment with Acridine of the Malaria Attack and its Suitability for Dispensary Practice]. *Settimana Med* 1946, Aug 3-31, Year 34, n.s., v 2, Nos 31/35, 64-8, 2 figs.

The 'standard' treatment of malaria attacks in Italy with Italchina [an acridine derivative, see this *Bulletin*, 1941, v 38, 34], has consisted hitherto

in the administration to patients 14 years of age and upwards, of 0.3 gm. a day for five days in *P. vivax* infections, and for seven days in *P. falciparum* infections. The authors report the treatment of 211 cases of *P. vivax* malaria and 54 cases of *P. falciparum* malaria with larger doses for a period of 4 days only in both types of infection the doses being 0.5-0.6 gm. a day for adults. The results are compared with those obtained by the treatment of 1813 cases by the "standard" method. The observations were made in an endemic area of Szech. The blood of all patients was free from parasites on the 4th day. In 98 per cent. of the *P. vivax* infections on the 3rd day. There was no significant difference in the incidence of relapses after the two methods of treatment. Symptoms of intolerance to the drug were absent or insignificant in the vast majority of cases. One patient developed transient psychotic symptoms.

The short system of treatment possesses obvious advantages for dispensary practice in rural areas especially and is recommended. Norman H. Kille

Pinto, G. de S. Sobre a ação da paludrina nos acessos de malária. [The Action of Paludrine in the Treatment of Malarial Attacks.] Reprinted from *Folha Ued.* 1947 Aug 25 12 pp

A severe outbreak of malaria in the early months of the year occurred in Itapema a district in the Guarujá município in the Isle of Santo Amaro near Santos Brazil. The outbreak was attributed to the influx of very large numbers of chronic malaria sufferers. (The vector *A. tritaeniorhynchus* was surprisingly difficult to find, only exceptionally being captured in houses.) About 90 per cent. of the infections were caused by *P. vivax*.

Paludrine was used in the treatment. 11068 patients with acute malaria. Of 557 patients treated with a single dose of 2 tablets, 0.20 gm. febrile symptoms were promptly suppressed in 89.4 per cent. When 4 tablets were given in two doses, the success rate was 97.7 per cent. (93 cases)

Norman H. Kille

Kierland R. R. & McCright W. G. The Termination of Therapeutic Malaria with Chloroquine. *Amer J Syph* 1948 Jan v 32 No 1 57-8.

The authors refer to previous work on the use of chloroquine in the treatment of malaria and especially in acute relapsing *P. vivax* infections this *Bulletin* 1948, 45-57.

They have used chloroquine to terminate therapeutic malaria in 3 patients suffering from central nervous syphilis who had been inoculated therapeutically with a strain of *P. vivax* which had been in use for more than 20 years. The inoculation took the form of an intravenous injection of 5 cc. of infected whole blood direct from patient to patient. The incubation period varied from 1 to 14 days and each patient had between 7 and 10 paroxysms before termination was attempted. The result obtained with chloroquine could not be shown to be affected by the incubation period or by the number of paroxysms.

Each patient was given 1 gm. of chloroquine followed in six hours by 0.5 gm. and then 0.5 gm. again in twenty-four and forty-eight hours (total 2 gm.). In two cases a total 1.3 gm. was given. The chance of relapsing was reduced when the drug was given after the paroxysm temperature had fallen below 103°F. and thus also reduced the likelihood of an additional paroxysm. In 1 case, no febrile episodes occurred after the treatment had started but in 4 an additional paroxysm occurred within twenty-four hours. In all these 4 cases the drug had been given when the temperature was rising.

Only one patient reported a side-reaction, namely a mild and transient gastro-intestinal upset no skin reactions were reported

In 14 cases in which the blood was examined for parasites after chloroquine had been given, parasites were found to have disappeared within 24 hours of the initial dose in 2, within 48 hours in 4 and within 72 hours in 7. In one case, the parasites persisted until the 5th day. One case was negative microscopically throughout. No relapses have been noted during follow-up periods of 2 to 8 months after treatment.

H J O'D Burke-Gaffney

CURD F H S GRAHAM W RICHARDSON D N & ROSE F L Synthetic Antimalarials Part XXII Some Quinolylamino-substituted Pyrimidine Derivatives *J Chem Soc* 1947, Dec 1613-19

DOUGLAS B JACOMB, R G & KERMACK, W O Attempts to find New Antimalarials Part XXVI Further Derivatives of *p*-Phenanthroline *J Chem Soc* 1947 Dec 1659-61

COVELL G A Brief Review of the History and Development of the more Important Antimalarial Drugs *Indian J Malariology* 1947 June v 1 No 2 231-41 [13 refs]

WALTON, G A On the Control of Malaria in Freetown, Sierra Leone I *Plasmodium falciparum* and *Anopheles gambiae* in relation to Malaria occurring in Infants *Ann Trop Med & Parasit* 1947, Dec, v 41, Nos 3/4, 380-407, 7 figs [56 refs]

The author was the first medical entomologist appointed to the Government of Sierra Leone. At that time, 1943, malaria control, on a large and comprehensive scale was begun as an urgent wartime necessity. By co-operation with the three Services, mosquito breeding in the western and eastern rural areas and Central Freetown was controlled by larvicides. An extensive network of mosquito catching stations indicated the anopheline house population from week to week. This paper is an assessment of the effect of these measures during the period June 1944-June 1946, on malaria incidence in Freetown.

Freetown has some 8,000 houses and population of 80,000, and is situated along a coastal plain less than a mile wide and backed by heavily wooded mountains. Humidity is high all the year and there is a heavy rainfall of about 130 inches per annum, five months are almost dry, but July and August have 35 inches each. That the house population of *Anopheles gambiae* was very markedly reduced is shown by the following table —

Number of female *A. gambiae* per 1,000 rooms per month in Freetown June 1944 to May 1946

June	July	Aug	Sept	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May
261	447	189	55	8	4	7	11	10	4	7	64
330	116	37	18	4	1	15	23	20	27	20	147

The anopheline infective density is a means of expressing the malaria-transmitting ability of an anopheline population. The number of infected *A. gambiae* for each average Freetown room from October 1944 to March 1945 is calculated at 0.07. In other words, there was on the average only one infected *A. gambiae* in every 14th room per 18 months. Applying this conclusion to the human population of Freetown for that period, one in 56 persons would receive an infected mosquito bite—this figure is a maximal estimation.

### Malaria in African Infants

*Parasite Infestation of Infants.*—Data of infestation placed in age-groups of 3 months and plotted semi-logarithmically is as follows —

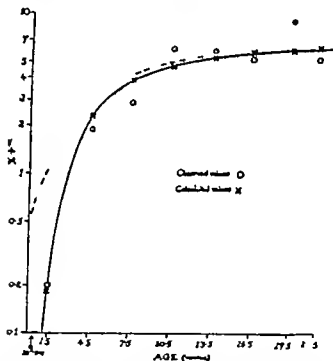


Fig. 1.—Graph showing the rate of increase with age in percentage malaria infestation of infants. The black curve is based on the recognition of not less than four trophozoites; the dotted curve includes all positive findings, but the true curve of infestation is probably even higher since some infections must have been missed. Fig. 7 is original.

*Effect of Mosquito Control.*—The comparable numbers of infected bites per room per year in an eastern rural suburb (Kissy) in 1931 and in Freetown in 1931 and 1945 were roughly .50, .30 and 0.07.

Parasite infestation in age groups in the same areas for the years 1931 and 1945 is illustrated as follows —

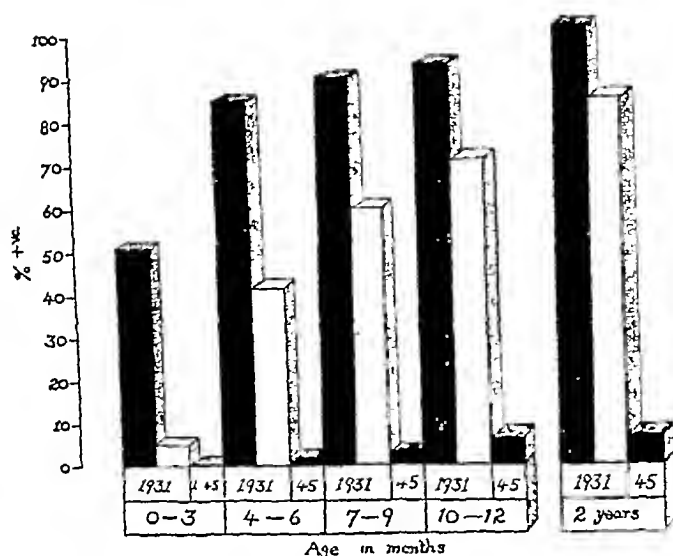


Fig 2—The effect of mosquito control on the parasite index of infants at different ages. The tall black columns show the parasite-indices of infants living in the rural village of Kussy close to Freetown in 1931; the white columns show the parasite index of Freetown infants in 1931; and the short black columns show the same for the period 1944-46. [Fig 5 in original]

[That this marked reduction occurred only in Freetown, and not also in the surrounding country, is shown by the work of Davidson in 1946; his summarized results for parasite indices in children were 80 per cent for coastal and 73 per cent for interior villages]

#### *Relation between the Anopheline Infection-Rate and the Malaria Parasite-Rate in Infants*

A statistical method is described for estimating the number of infective mosquito bites and the associated parasite-indices; the calculated result is summarized in Table VI below.

**Rate of Infection of Infants**—It was possible to keep track of 50 infants for eighteen months or more; 12 to 15 infections were received, that is 1 in 4. The considerable discrepancy between this figure and the above-mentioned 1 in 56 persons is believed to be due to infections acquired outside the controlled area.

**Duration of Infection in Infants**—A table summarizes monthly blood examinations of 31 infants up to the 24th month. The difficulty of following-up cases has caused many omissions, but the data do throw some light on the duration of single infections; the average appears to be about 9 months.

**Gametocyte Production**—It was observed that gametocytes appeared for one month only, during which trophozoites were suppressed. The mean number of trophozoites unaccompanied by gametocytes was 1,000 per 150 fields, while the mean number with gametocytes was 14.

TABLE VI

Parasite indices produced group young children by various numbers of anopheline mosquito-bites per day

No. of infective bites per child per year	Calculated parasite-rate per cent in young children
0-01	0.21
0-10	57
0-20	5.07
0-30	7.50
0-40	9.90
0-50	12.20
0-70	16.60
1-00	22.90
1-50	33.30
2-00	40.50
3-00	54.20
4-00	64.0
5-00	73.0
7-00	83.60
10-00	94.00
20-00	99.45
30-00	99.96
50-00	99.99

*Sensitivity of Infants*—From the data available it would appear that contrary to what would be expected the intensity of infection, as measured by the number of trophozoites in the blood, increases with age at least up to the age of 15 months. Apparently the infants become increasingly susceptible as they grow older. The figure below attempts to portray the change in parasite quantity with age.

*Previous Work*—A summary is given of previous work in the light of this and his own experience the author concludes that, for some reason, very young infants are not bitten by anophelines to the same extent as older children or that when bitten by infective mosquitoes, they possess some mechanism which prevents the appearance of plasmodia in the peripheral blood.

Whatever brings about active proliferation of the reticulo-endothelial system of the mother might well do the same to the unborn child and hence the newly born infant would be ready to deal with its first infection.

[The author has made most valuable contribution to knowledge of malaria transmission in addition to proving the efficiency of larval methods of control when backed by sound organization he claims a virtually 100 per cent. effective result. This information with a full list of references, requires to be digested in the original by readers interested in the subject.]

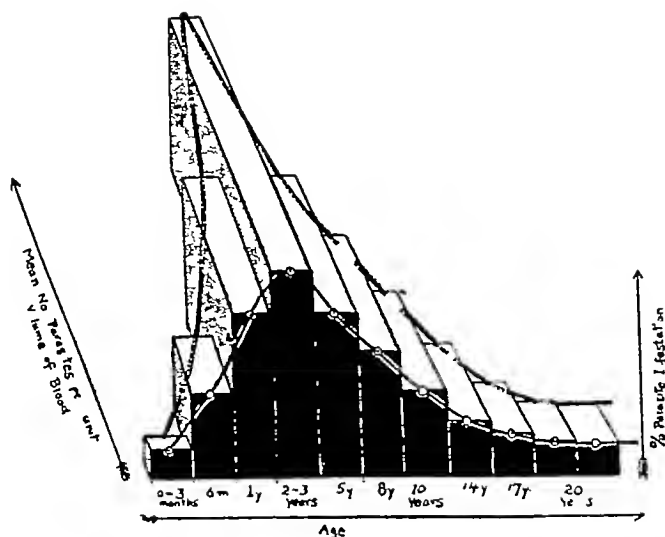


Fig 3—Three-dimensional hypothetical representation of the variation of intensity of parasite infestation at different ages

The horizontal axis shows age increasing from left to right the older age groups are foreshortened. Based on the age group scale the histogrammatic representation in the vertical axis depicts the change in percentage parasite infestation with age. Superimposed on this is the graphic representation of the same data. The depth of the receding columns represents the mean number of parasites per unit volume of blood (intensity) in each age-group the scale being on a horizontal axis at right angles to the axis depicting increasing age. The differences in the intensities of parasite infestation at different ages are greatly reduced nevertheless the great variation in the degree of parasitization at different ages is quite clearly shown. The receding curve passing through the distal margins of the columns represents the change in parasite quantity with age [Fig 6 in original]

[Figures reproduced from the *Annals of Tropical Medicine and Parasitology*]

R Ford Tredre

THOMSON, R C Murhead. The Effects of House Spraying with Pyrethrum and with DDT on *Anopheles gambiae* and *A. melas* in West Africa. *Bull Entom Res* 1947, Dec, v 38, Pt 3, 449-64 [23 refs]

*A. gambiae* and *A. melas* are well known house-frequenters by day, but the author submits evidence of out-door resting places and is of opinion that the number of mosquitoes caught by routine methods in houses by day may be only a small proportion of the mosquitoes actually feeding there at night. Ninety per cent of feeding by *A. melas* and *A. gambiae* takes place between midnight and dawn, and it is possible for the mosquito to spend only an hour or two of the 48-hour gonotrophic cycle in the house.

Three villages near Lagos were mass-sprayed with "Pyefly" diluted 1 in 59 with kerosene, at the rate of  $\frac{1}{2}$  to  $\frac{3}{4}$  ounce per 1,000 cu ft, with the results shown above. In the selection of these villages, care was taken to ensure that there was no infiltration of infected mosquitoes from other areas. Even the intensive spraying of the last period failed to bring about a substantial reduction

## Spray-killing in Houses with Pyrethrum in Kerosene

TABLE I

Mass spraying of village houses with pyrethrum in kerosene. Incidence and fecundity of malarial and gambian. December 1942-April 1943

Treatment	Number and period of collections	Gambian and malarial per 10 bed-rooms	Mosquitoes dissected	Glands positive	Sporozoite rate
Preliminary survey Houses untreated	8 18/iii to 19/i				Percent.
All houses sprayed four times weekly from 19/i	13 1/ii to 7/ii	33	485	17	3.5
All houses sprayed six times weekly from 7/ii	7 14/ii to 2,iv	11	403	12	3.0
All houses sprayed six times weekly from 7/ii		12	47	18	7.3

in the numbers of mosquitoes in houses, though the increase in the sporozoite rate may be due partly to the increase in breeding of *A. gambiae* expected at this time of the year.

As a result of the use of experimental huts provided with suitably designed window traps in an area infested with *A. malaris* evidence is offered to explain the results of village spraying. In short, in an untreated hut of the local type the number of blood-fed female mosquitoes found resting by day represent  $\frac{1}{3}$  to  $\frac{1}{2}$  of the total numbers feeding there the previous night but in the hut sprayed daily with pyrethrum in kerosene the numbers found in the hut by day represent only  $\frac{1}{3}$  of the total feeding there at night. Pyrethrum in kerosene has an irritant effect on many blood-fed *A. malaris* driving them out of the house after feeding. It also has a repellent effect, but it discourages entrance to the house only if an alternative untreated house is a viable female *A. malaris* are not attracted to animals nor are they driven to animal feeding by mass spraying of human habitations they prefer to enter the latter at night to feed and leave almost at once. As a corollary to these conclusions the author observes that however efficient spray killing may be in estimating the total house or room-catch it should not be used in the same house more than once a week, otherwise the results may be affected by a shift of mosquitoes from inside the house to outside resting places.

The author concludes —

The fall in the number of mosquitoes resting by day in houses after spraying is now seen to be caused, not by any great reduction in the population as a whole but rather to a shift from indoor to outside resting places. The number of mosquitoes killed by even the most intensive spraying represents such a small proportion of the whole that the average length of life may be little affected, the parasite rate remaining at much the same level as before.

## DDT as a residual insecticide

In the light of the observations on pyrethrum the author proceeded to the investigation (by similar methods) of the effects of DDT in kerosene as a residual insecticide. The mass treatment of village houses by the usual methods produced the expected result namely that house catches fell practically to zero and remained low for the nine weeks of observation.



Behaviour of *A. melas* in Experimental Huts

TABLE V

Treatment of experimental huts with DDT One hut treated at rate of 100 mgm DDT per sq ft Other hut untreated Catches refer to freshly blood-fed *Anopheles* (95 per cent *melas*, 5 per cent *gambrie*) Window traps record mosquitoes leaving hut after feeding

	Before treatment	After spraying					
		1 Week	2 Week	3 Week	4 Week	5 Week	6 Week
Number of visits	8	5	5	6	6	3	4
Treated hut { Hut catch	77	0	0	1	0	1	0
Window trap	27	44	89	176	255	133	178
Untreated hut { Hut catch	91	189	244	390	140	138	194
Window trap	25	56	12	223	294	123	35

TABLE VI

As in Table V but experimental hut treated at rate of 250 mg DDT per sq ft

	Before treatment	After spraying			
		1 Week	2 Week	3 Week	4 Week
Number of visits	5	4	6	5	3
Treated hut { Hut catch	189	0	0	0	0
Window trap	56	2	28	157	82
Untreated hut { Hut catch	273	196	390	115	138
Window trap	40	10	223	245	123

No dead *Anopheles* were found on the floor-matting of the treated hut, the mortality, during 48 hours after feeding, among mosquitoes leaving the hut was practically nil. By a separate experiment, it was shown that the absence of mosquitoes from the hut for ten days after treatment is more likely to be due to the repellent effect of a heavy dosage of kerosene than to the presence of DDT.

In the case of an isolated village, outside resting-places had been found and kept under observation for many months, 113 *A. melas* caught in these outside resting-places had a sporozoite rate of 2.7 per cent. During a period of five weeks after treatment of the village with DDT in kerosene (200 mgm DDT per sq ft), 295 blood-fed and gravid mosquitoes were caught in the outside resting-places, with a sporozoite rate of 2 per cent, infected mosquitoes were still found at the 5th week.

#### Conclusion

The sharp fall in house catches after treatment with DDT in kerosene does not necessarily mean a corresponding reduction in mosquito population or biting activity. The most obvious effect of the treatment is to bring about a

complete shift from indoor to outside resting places. Furthermore the sporozoite rate of those mosquitoes caught outside is such as to suggest that malaria transmission is still possible.

[This work rightly draws attention to the fallacies associated with the indiscriminate use of DDT in kerosene applied as a residual insecticide in West Africa. Health officers there might well infer that the residual insecticide method is valueless as a measure of malaria control. On the contrary the author's valuable paper should stimulate further investigation.

Ling Gammexane in Kerosene in Sierra Leone DAVIDSON (this Bulletin 1948, v 45 157) produced evidence to show that the treatment of houses in part of an area reduces the mosquito population, not only in that part but also in adjacent parts one to two miles distant. The area concerned was a coastal strip six miles long, with a string of seven villages, of which the first, third and sixth were untreated. Similar results were obtained in a group of inland villages.]

R. Ford T. cit.

PEIXIDO H. M., AZEVEDO N., PINTO D. B., BEZERRA, F. Jr. & MOURA, F. P. Malaria do vale do rio Doce. Organização e execução de serviços antilariários. [Malaria in the Valley of the River Doce: Organization and Activities of the Antilarial Services.] *Rev. Hig. e Saúde Pública* 1947 July-Sept., v 5 No 2, 3-25 2 maps.

This paper describes in detail the antilarial work carried out in the valley of the River Doce in the State of Minas Gerais from August 1943 to June 1947 (see above). Here *A. darlingi* is the sole vector. Chief reliance was placed on Paris green. The marked decline in malaria prevalence in certain places indicates the success achieved.

Norman H. cit.

BRAGA, E., PEIXIDO H. M., BASSIRES M. S., PINTO D. B., BEZERRA, F. P. Jr. & MOURA, F. P. Malaria do vale do rio Doce. Espurgo domiciliar com DDT em suspensão aquosa. I fase. [Malaria in the Valley of the River Doce: Treatment of Habitations with Aqueous Suspension of DDT.] *Rev. Hig. e Saúde Pública* 1947 July-Sept., v 5 No 2, 26-59 3 maps & 3 charts. 14 refs.

In September 1946 the DDT spraying of houses was commenced as an antimalaria measure along 120 kilometres of the Vitória-Minas Railway in the most malarious parts of the valleys of the River Doce and Piracicaba in the State of Minas Gerais (see above). The width of the area treated varied from 3 to 15 kilometres. The total area was about 1,500 square kilometres containing a population of about 20,000 in 5,000 houses. An aqueous suspension of DDT was applied (5 per cent) at the rate of 2 gm. per square metre. In January 1947 a second application was begun. About 85 per cent of all houses were treated. The almost complete absence of *A. darlingi* from houses treated, a marked fall in the number of malaria parasite carriers and a very notable fall in the number of persons applying for treatment for malaria, testify to the noteworthy success achieved. Very full details are given of the work carried out.

Norman H. cit.

GRAMICCIA, G. & ACCI, G. Not sulla infezione da *P. gallinaceum* nel pulcino. Considerazioni sul significato biologico del ciclo endossicotico dopo inoculazione di sangue. [Biological Significance of Exoerythrocytic Cycle of *P. gallinaceum* in Young Chicks.] *Arch. di Parasit.* Rome 1947 Dec. v 8, No 4 213-19. English summary.

The inoculation of young chicks 5-8 days old with blood infected with *P. gallinaceum* produces more severe infection than when adult chickens are

inoculated The young chicks first show exoerythrocytic forms on the 11th day of the blood infection, which is always fatal The author interprets this period of eleven days as a cycle wherein the parasite attempts to repeat those phases that were omitted because of the method of inoculation In the case of *P. elongatum*, blood inoculation is followed at the same time by both erythrocytic and exoerythrocytic development, while in the case of gametocytes these appear after a number of erythrocytic cycles

C M Wenyon

TOKIN, I M & HAWKING, F Growth of Protozoa in Tissue Culture  
IV *Plasmodium lophurae*, Exoerythrocytic Forms, *in vivo* and *in vitro*  
*Trans Roy Soc Trop Med & Hyg* 1947, Dec, v 41, No 3, 407-14,  
23 figs (16 on 3 pls)

By means of sporozoites obtained from *Aedes albopictus* infected by feeding on chickens harbouring *Plasmodium lophurae*, infection was produced in young turkeys The observations of PORTER and LAIRD were confirmed that infection of the turkeys was associated with the production of exoerythrocytic schizonts which resembled those of *P. gallinaceum* With spleen material removed from one bird tissue cultures were made These resulted in the development of exoerythrocytic schizonts which again resembled those obtained by tissue culture of *P. gallinaceum* The exoerythrocytic schizonts showed both macro- and micro-merozoite formation The various stages in sections of tissues of the young turkeys and in the tissue cultures are illustrated in a series of black and white drawings and many other forms are shown in photo-micrographs

C M Wenyon

RIGDON, R H & McCAIN, B E Some Factors that Influence the Degree of Parasitemia in Ducks Infected with *P. lophurae* *Amer J Trop Med* 1947, Nov, v 27, No 6, 673-81, 7 figs [19 refs]

Young ducks 2-4 weeks old, when given a lethal dose of *P. lophurae* die at the height of the parasitaemia or when the parasites are decreasing in number Some ducks, however, survive the infection, which may reach a figure of 400 infected cells per 500 red blood corpuscles on the 5th day of infection In the survivors, the number of parasites rapidly decreases, so that in 48 hours only 5-10 parasitized cells per 500 red blood corpuscles are present These ducks rapidly return to normal and within 5-7 days show no abnormalities in their haemogram It seems improbable that the cells of the reticulo-endothelial system which are filled with pigment at the crisis are able to remove from the circulation the large number of parasites then present

It has been shown that ducks with polycythaemia have larger numbers of parasites than normal ducks, while transfusion of infected ducks with normal red blood cells will prevent the decrease in the parasites which follows the peak of the infection Another factor which will increase the number of parasites is oxygen for ducks placed in a chamber with a concentration of oxygen of 30-80 per cent show a greater number of parasites in the peripheral blood Again *P. lophurae* prefers mature red blood cells to those that are young and there is a marked diminution of adult cells when the parasitaemia is high These young cells are poor in haemoglobin and the oxygen-carrying ability of the blood decreases during the infection

It has recently been shown that if blood for inoculation is treated with CO<sub>2</sub> by bubbling the gas through it, many of the parasites are so altered that it fails to produce the same degree of parasitaemia as when oxygen or nitrogen are bubbled through it Observations have shown that malaria-infected ducks develop a severe acidosis which is directly related to the anaemia The

CO<sub>2</sub> content of the plasma however remain approximately normal until the anaemia falls to below one million, after which it declines steadily till the time of death. After the administration of ammonium nitrate to ducks, there occurs a severe acidosis with no anaemia, while there is a decrease in the CO<sub>2</sub> content of the plasma. Administration of sodium bicarbonate is followed by a severe alkalosis with only slight anaemia and increase in the degree of retention of CO<sub>2</sub>. It is concluded that the acidosis which occurs in malaria may not result entirely from the anaemia, since ducks with an acidosis following ammonium nitrate administration have no anaemia. To determine the relation of the total number of red cells to the CO<sub>2</sub> in the plasma, the CO<sub>2</sub> content was divided by the number of red cells in millions. This factor was plotted against the total number of red cells. A similar factor was obtained from ducks which had received ammonium nitrate and sodium bicarbonate. The points in the chart for the ducks with malaria parallel those of the ducks which had sodium bicarbonate. When the figure given by dividing the CO<sub>2</sub> content of the plasma is plotted against the number of parasitized red cells, it is found that the CO<sub>2</sub> content increases with the number of parasitized red cells. The greatest increase occurs when the parasitized cells number 250 or more per 500 red cells. It is thought that the CO<sub>2</sub> content may be sufficient to injure or kill some of the parasites.

C. M. Wrayson

### TRYPANOSOMIASIS

HARDING R. D. & HUTCHINSON M. P. Sleeping Sickness of an Unusual Type in Sierra Leone and its Attempted Control. *Trans. Roy. Soc. Trop. Med. & Hyg.* 1940, Jan. v 41 No 4 451-512, 1 map

In 1939 and 1940 medical surveys showed that sleeping sickness existed in an area of about 700 square miles on the eastern boundary of Sierra Leone adjoining French Guinea where the disease had been treated since 1934. Mass campaigns were decided on and were carried out in 1941, 1942 and 1944.

Sleeping sickness in Sierra Leone is caused by *Trypanosoma gambiense* and is spread by the bite of the tsetse fly *Glossina palpalis*. In the campaigns the focus was made by microscopical examination of the fluid obtained by puncture of enlarged superficial lymphatic glands and of blood films but as trypanosomes were found in the glands four times as often as in the blood, the latter was only examined when gland puncture gave negative results or when the glands were not palpable.

In 1941 the disease was clinically like that in other parts of Sierra Leone but in 1942, in the central part around the town of Freetown some differences were observed. Trypanosomes were found in the blood as often as in the glands and were unusually numerous in the blood. In some persons many patients had no enlarged cervical glands and showed no symptoms even when the blood contained many trypanosomes. All the inhabitants were examined and all cases of sleeping sickness were treated, but no further work was possible for a year. A survey in 1944 showed that the unusual form of the disease ("Freetown type") had spread considerably and the infection rate was nearly doubled. In Freetown itself, trypanosomes were found in the blood ten times as often as in the glands but in 1945 this disparity was less.

Seventy-five patients were left untreated and examined weekly for 6 months and 17 others, also untreated, were examined monthly for 7-9 months. Nearly all showed no symptoms or physical impairment. Trypanosomes appeared in the blood irregularly and it was reckoned that about 35 per cent. of cases would escape diagnosis at any single examination. Even patients with an increased

cell-count in the cerebrospinal fluid often had no symptoms. There seemed to be a state of equilibrium between host and parasite and some spontaneous recoveries probably occurred, but observation for several years would be required to confirm this. Although from a quarter to a third of the population of Fwero had been infected, the population had not decreased.

In experimentally infected monkeys the disease was also mild, in infected guinea-pigs the trypanosomes were resistant to intraperitoneal injections of human blood serum and sensitive to tryparsamide—characters of *T. gambiense* [Injection of human serum into guinea-pigs infected with *T. rhodesiense* will, in certain doses, banish the trypanosomes for several days].

**Prophylaxis**—The population (15,550) of the whole area received prophylactic injections of antrypol (germanin) or pentamidine isethionate and special observations were made of the 2,500 inhabitants of the central part, including Fwero, all the latter were examined by gland puncture and blood films and lumbar puncture was done in nearly all infected persons. Some of the sleeping sickness cases were fully treated, others left untreated, and still others received prophylactic doses of antrypol or pentamidine to see whether this would suppress the infection. A prophylactic injection was given to 1,765 uninfected persons and 542 were left as controls. The results with various prophylactic doses are shown in tables.

In infected persons given prophylactic doses, the blood showed no trypanosomes for at least 7 months, therefore missed cases of infection receiving a prophylactic dose would hardly infect tsetse flies during that period but their recognition later would be difficult and they might eventually become infective. No gland infections and only 2 blood infections were found after 7 months among 1,498 uninfected persons examined who had received prophylactic injections—a rate of 0.1 per cent—while among 471 controls there were 12 gland infections and 12 blood infections (5.1 per cent).

In two other areas of Sierra Leone, where sleeping sickness of the usual type was present, prophylactic injections proved very effective, after 1–2 grammes of antrypol, only 2 cases occurred among 772 people (0.26 per cent) and after 100–300 milligrammes of pentamidine no infection was found among 921 people while among 2,407 controls 22 cases (0.92 per cent) occurred. The period of observations in these investigations was 10 months.

The authors discuss the results and conclude that prophylaxis by drugs is more effective than treatment of cases in checking an epidemic and acts more quickly. Pentamidine is preferable to antrypol, being at least as efficient and having fewer undesirable side effects, a single intramuscular dose of 150 milligrammes is the best for a mass campaign. The importance of the possible masking of symptoms by prophylactic injections remains undecided.

J. F. Corson

GELFAND, M. Transitory Neurological Signs in Sleeping Sickness. *Trans Roy Soc Trop Med & Hyg* 1947, Oct, v 41, No 2, 255–8.

The author (writing from Salisbury, S. Rhodesia) discusses the usual symptoms and signs which indicate involvement of the nervous system in sleeping sickness, remarking that these are changes in personality rather than true neurological signs. This is to be expected in view of the fact that the disease is essentially a form of encephalitis, pathologically not unlike general paralysis of the insane. If paralyses do occur, they are usually not extensive, and the author has been unable to trace any record of transient paralyses in sleeping sickness. He now describes a case in an adult African, in which symptoms pointed to a form of encephalitis or tuberculous meningitis, with swelling of the right optic disc, a right extensor plantar response, and, shortly afterwards, a

right facial palsy which disappeared spontaneously in about 2 weeks. At this time no definite evidence of trypanosomiasis could be obtained, but about 6 weeks later the gradually worsening symptoms led to another examination of the spinal fluid, in which trypanosomes were now abundantly found. The type of disease was not definitely determined, but was probably *Rhodocytus*. Treatment with trypanarsamide and pentamidine was successful, but the patient left hospital when the course was completed, and his later history is not known.

Charles Wilcock

VAN HOOFF L. HENRIARD C. & PERL E. Notes sur l'action curative et préventive de la propamidine. [The Therapeutic and Prophylactic Action of Propamidine.] *Ann. Soc. Belge de Méd. Trop.* 1947 June 30 v 27 No. 2, 257-63.

The authors describe their experiences in the treatment of different types of sleeping sickness cases in Léopoldville. Propamidine (isethionate) was used in daily doses of 1 to 2 mgm. per kilo intramuscularly till a total of 25 mgm. per kilo was given in 5 hospitalized patients thus treated in 1943: no relapse occurred. In one arsenic resistant case with a moderate increase in leucocytes in the cerebrospinal fluid a return to normal had not taken place at the time of writing and one non-arsenic resistant case did relapse. Further cases responded less well to treatment and trypanosomes disappeared but slowly from the peripheral blood. Immediate toxic effects from the drug were of minor importance but paralysis occurred later in some cases. Nervous symptoms appeared to be avoidable if the drug were given intramuscularly. The authors confirm the abortive action of the drug described below by EERAERTS. Prophylactic experiments on guineapigs with a single dose of propamidine gave similar results to those previously obtained by the authors with pentamidine (this Bulletin, 1944 v 41 928). In human cases, the protection afforded by 5 mgm. per kilo was estimated to last 6 months as with pentamidine. The two drugs thus appear to have comparable protective and curative properties against *T. gambiense* infections but propamidine seems to be more toxic, giving rise to paresis and paralysis.

J. D. Fulton

EERAERTS W. La propamidine comme préventif dans deux foyers de trypanosomiase humaine au Congo Belge. [Propamidine as a Preventive in Two Foci of Human Sleeping Sickness in the Belgian Congo.] *Ann. Soc. Belge de Méd. Trop.* 1947 June 30 v 27 No. 2, 201-24. [20 refs.]

The author refers to the earlier work of VAN HOOFF *et al.* (this Bulletin 1944 v 41 928 1948 v 43 536) on the value of pentamidine in prevention and treatment of Gambian sleeping sickness in the Belgian Congo. He himself has carried out comparable field trials with propamidine in two active foci of infection in the Kwango district of Léopoldville province. Two injections of the drug in 4 per cent. solution were given deeply into the muscles, with an interval of six months between doses. For adults the maximal dose was 5 mgm. per kilo (presumably of isethionate) with gradations according to age. In all, about 8 000 Africans were injected, none of whom was clinically ill. At the time of the first injection, the disease was spreading rapidly in one district. Examinations were made at intervals of 2 or 4 months after the injections and again at the end of six months, when no infection could be found in those who had received the drug. Four and nine months after the second injection the same state of affairs held. In a second focus of infection the trypanosomes were arsenic-resistant and the disease was spreading rapidly with 23.5 per cent. of new cases in a total of 41.1 per cent. of the population infected. Three and six

months after injection with propamidine, no fresh cases were present among those treated. From his experiments the author concluded that protection lasted from 6 to 8 months

The drug does not clear the peripheral blood rapidly and he considers its chief rôle to be that of a preventive rather than curative agent. There were some minor toxic symptoms from the drug, including epigastric pain, transient albuminuria and mild paresis of limbs. Two aged patients exhibited more serious signs of intoxication, including lowered blood-pressure, tachycardia, dyspnoea, severe epigastric pain and coma, but recovery was complete after 12 hours. The abortive action of propamidine has not previously been recorded since smaller doses of the drug have generally been used. The large dose of 5 mgm of propamidine per kilo, however, brought about this result in a large percentage of pregnant women. Half this dose was well tolerated.

The mechanism of the protection afforded by propamidine is not yet clear, but the practical achievement of wiping out one focus of infection and nearly eradicating another is of the utmost importance. The results compared favourably with those obtained by the use of Bayer 205, and advantages claimed for propamidine over Bayer 205 are its greater solubility and lesser toxicity, as well as the fact that it can be given intramuscularly

J D Fulton

WILLIAMSON, J & LOURIE, E M "Melarsen" and "Melarsen Oxide"  
*Nature* 1948, Jan 17, 103-4 [14 refs]

VAN HOOF [this *Bulletin*, 1947, v 44, 1048] found that melarsen oxide, a new type of phenylarsenoxide containing a melamine group, was active against arsenic-resistant trypanosomes in the field. His findings have been confirmed by the present authors in the laboratory. They point out that arsenic resistance in the case of trypanosomes in fact involves resistance to the substituted phenyl group to which the arsenic is attached. It was recognized in the earliest investigations that trypanosomes made resistant to atoxyl failed to exhibit this property on treatment with aromatic arsenicals containing acidic groups. KING & STRANGEWAYS [this *Bulletin*, 1943, v 40, 20] suggested three ways in which the different types of aromatic arsenoxides may be distributed in or on the trypanosome, while the final reaction in which the parasite was killed probably involved in all cases combination between the arsenoxide and sulphhydryl groups in the trypanosomes. Interference experiments were used to provide evidence that melarsen oxide may combine with the trypanosome in still another way. Thus melamine itself and Surfen C, which also contains a melamine group, were found to interfere with the therapeutic action of melarsen oxide on a normal strain of *T. rhodesiense* as did *p*-aminobenzoic acid with that of  $\gamma$ -(*p*-arsenosophenyl) butyric acid and glutathione with arsenoxides in general. The authors conclude that the mode of combination between trypanosomes and melarsen oxide is different from that of other arsenoxides, although the final lethal effect of the latter is produced in the same way. The interference between melarsen oxide and Surfen C appears to depend on the common possession of a melamine group

J D Fulton

VANDERPLANK, F L Seasonal and Annual Variation in the Incidence of Trypanosomiasis in Game *Ann Trop Med & Parasit* 1947, Dec, v 41, Nos 3/4, 365-74 [15 refs]

These investigations were made in Tanganyika Territory from June 1939 to June 1944, 378 wild mammals belonging to 38 species were shot and their blood examined microscopically for the presence of trypanosomes. The results

In 135 of them (153 in the text) were recorded in a previous paper (*Trans. R. Soc. Trop. Med. & Hyg.* 1942, v 35 319). Similar observations by E. F. THOMSON in Northern Rhodesia are also shown in a table.

Giraffes showed the highest rate of infection (37 per cent.) then roan, eland, zebra, impala and wart-hog in that order while no trypanosomes were found in carnivores, monkeys and rodents. *Trypanosoma congolense* (*T. simus*?) was found in 1 of 6 elephants. There were no significant differences in the rates of infection between young and adult animals nor between the sexes. The rate varied with the season, being highest in March and April, the time of heavy rain, and it varied also from year to year in correlation with annual variation in the proportion of infected wild tsetse flies. The animals were far more often infected with *T. congolense* and *T. vivax* than with *T. brucei*, the rate of the last being less than 1 per cent.

Wild tsetse flies, *Glossina swynnertoni* and *G. pallidipes* were dissected and examined and the following rates of infection with trypanosomes were found among 33 112 flies: *T. congolense* 2.2 per cent., *T. vivax* 2.1 per cent. and *T. brucei* less than 0.1 per cent. The author found (unpublished work) that temperature markedly affected the transmissibility of *T. rhodesiensis* and *T. congolense*. The activity and hunger cycle of tsetse flies and their apparent and actual numbers were also investigated.

The erythrocytes of blood recently imbibed by 1,600 *G. swynnertoni* were measured and the results indicated that this species feeds largely on giraffes and large antelopes, some observations by the author (this Bulletin, 1944 v 41 1010) showed that *G. pallidipes* preferred to feed on pigs.

Various kinds of wild animals were experimentally infected with *T. rhodesiensis*; wart-hogs rarely showed trypanosomes in the blood, but rats were infected from them by inoculation. Trypanosomes appeared in the blood of elands for several days at a time up to 6 months after the infecting bite and a goat was infected by inoculation of 50 cc. of blood from an eland infected as previously. Other animals showed various degrees of infection. J. F. CORRIE.

WILDER, J. K. H. The Maintenance of Cattle under Conditions of Tsetse Fly Infestation in the Field. *J. Comp. Path. & Therap.* 1947 Oct., v 57 No. 4 294-300. 1 sketch map.

This experiment was made to see whether cattle could be kept in good health by the use of drugs in a district in Tanganyika Territory where clearing work to get rid of tsetse flies was in progress, but would not be able to eliminate the flies for a long time. It also served to test the value of two drugs—No. 897 (a compound of phenanthroline chloride) and Stibophen (antimony). The experiment began in September 1944 and lasted for 14 months.

A number of cattle (153) were divided into 5 herds (A, B, C, D & E) which were then stationed at 4 different places respectively in the area. Their blood was examined microscopically every fortnight for trypanosomes and the drugs were used prophylactically and to treat infections. In herd A (11) infected animals received Stibophen twice with a week interval between the doses; in herd B (31) infected animals received one dose of No. 897; herd C was subdivided into groups a, b and c for treatment but all were kept together in a (15) all got Stibophen once a month, in b (16) all got No. 897 once a month, and in c (15) infected animals got No. 897 after each fortnightly post-mortem blood film; in herds D (25) and E (40) No. 897 was given each when a blood film was positive.

Infections were arbitrarily called new, as distinguished from relapses, if a positive blood film had been preceded by two fortnightly negative blood





female mice as judged by trypanosome population in the blood, degree of tissue infection, loss of body weight and survival of the host. C. M. Weryne

MUNIZ, J. & DE AZEVEDO, A. P. Novo conceito da patogenia da "doença de Chagas" ("Trypanosomíase Americana"). Inflamação alérgica granulomatóide (A) e miocardite hiperérgica (B) produzidas em Rhesus ("Macaca mullata") inoculados com formas mortas de cultivo do *Schizotrypanum cruzi* (Nota prévia.) [New Conception of the Pathogenicity of Chagas's Disease.] *Hospital* Rio de Janeiro, 1947 Aug. v. 32, No. 2, 165-83 8 figs. [22 refs.] English summary

The authors have studied the pathogenicity of *Trypanosoma cruzi* by sensitizing two monkeys by intravenous injections of a protein-free antigen and then administering a shock injection. The antigen was prepared from cultures grown on solid medium. After the flagellates were washed with saline solution they were dried at a temperature of  $-70^{\circ}\text{C}$ . They were kept dry at a temperature of  $-10^{\circ}\text{C}$ . or in suspension in distilled water.

To carry out the test, two rhesus monkeys received five intravenous injections of the antigen at intervals of 3 days, two of the injections being 0.040 gm. and three 0.045 gm. Twelve days after the last injection, a shock injection of 0.010 gm. of antigen was given directly into the pleura and the cardiac region. One of the animals was given three further injections of the sensitizing antigen. One of the monkeys was killed eight days after the shock injection and the other 33 days after. Before being sacrificed, both monkeys gave ++++ precipitin reaction according to the method of Muniz and Freitas. As controls, two monkeys were given injections of antigen without a shock injection.

Examination of the pleura and cardiac tissues of the monkeys showed that inflammatory reactions were set up, there being a similarity of the histopathological picture to the lesions in Chagas's disease. In the control monkeys, such lesions did not occur. The experimental result supports the conclusion of TORRES that there is an allergic condition in the pathogenesis of the disease. C. M. Weryne

VALLS, D. J. Contribuciones al estudio de la enfermedad de Chagas. VI. Estudio cardio-vascular de enfermos de trypanosomíasis Americana. [Chagas's Disease. Cardiovascular Study.] *Rev. Chilena de Hig. y Med. Preventiva*, 1947 June v. 9 No. 2, 189-219 7 figs. on 6 pls. [53 refs.]

In this study the author first carried out xenodiagnostic tests—any persons found positive were then examined clinically to exclude those with other common causes of cardiac disturbance—valvular lesions, arterial hypertension, hyperthyroidism, etc. The districts where the examinations were carried out were rural and heavily infested with *Triatomidae*.

The author analysed 411 cases—so stated repeatedly—but in a table giving the age and sex of the patients the total should be 417—the numbers of males in one district, San Enrique, being wrongly added and in another column the age distribution total is again wrong. Of 397 electrocardiograms, there were 123 with sinus arrhythmia, 11 with A-V block 6 with ventricular extrasystole (most of these patients were young—4-18 years of age) and 5 with supraventricular extrasystole. In spite of this, there seemed to be little if any general disturbance of health or limitation of capacity to work. Details as given of 18 cases and in an appendix a general scheme is laid down for clinical study of Chagas's disease noting the points to be looked for and the various laboratory tests to be carried out (xenodiagnosis, Machado reactions, etc.) autopsies should be made when permitted, otherwise necropsy samples should be taken. H. Harad Sci. 3

AUGUSTINE, D L Experimental Studies on Trypanosomiasis (*Trypanosoma lewisi*) *Liber Jubilaris J Rodham* (Soc Belge Méd Trop, Brussels) 1947, Dec, 63-80, 3 figs

The substance of this paper appeared in an earlier publication by the author [this *Bulletin*, 1946, v 43, 1025] C M Wenyon

CALDWELL, F E & GYÖRGY, P The Influence of Biotin Deficiency on the Course of Infection with *Trypanosoma lewisi* in the Albino Rat *J Infect Dis* 1947, Nov-Dec, v 81, No 3, 197-208, 1 fig [25 refs]

It has been shown by various workers [this *Bulletin*, 1943, v 40, 825, 891, 1944, v 41, 651, 1945, v 42, 540, 864] that the course of a protozoan infection may be modified by deficiency of certain vitamins in the host. The effect of biotin deficiency on the course of *T lewisi* infection in rats has now been further investigated by the present authors. To produce this deficiency, one group of animals was given a modified egg-white diet supplemented by other vitamins. Another group received a linoleic acid diet involving a toxic factor and a low protein intake which was also supplemented by other vitamins and did not increase susceptibility to *T lewisi* infection. The degree of biotin deficiency was assessed from the appearance of the animals. A standard number of trypanosomes, based on body weight, was used for inoculation. Red cell as well as parasite counts were made regularly up to some days after the disappearance of parasites. Death from bacterial and other causes was common in the deficient groups, and all had more severe infections than the controls, while death from very intense infections occurred in moderately deficient rats. When adequate amounts of biotin were given subcutaneously to the latter, the development of trypanosomes was not immediately controlled. Excess biotin given to normal rats likewise exerted no protective or curative action. Treatment with hyperimmune serum caused the trypanosomes to disappear within 24 hours in non-deficient rats, but not in the deficient rats, which later succumbed to the infection. A deficiency of complement in their serum was indicated. The results suggest that biotin deficiency caused delayed and diminished production of ablastin as well as of trypanolysin, so that an intense and prolonged infection resulted. J D Fulton

DEANE, Maria P Ocorrência do *Trypanosoma conorrhini* em "barbeiros" e em rato na cidade de Belém, Pará, e seu cultivo em meio de NNN [Occurrence of *Trypanosoma conorrhini* in "Kissing-Bugs" and a Rat in Belém, Pará, and its Cultivation on NNN Medium] *Rev Serviço Especial de Saúde Pública* Rio de Janeiro 1947, July, v 1, No 2, 433-48, 70 figs on 6 pls English summary

The "kissing-bugs" in question, which were found in houses in the "Cidade Velha" section of Belém, Brazil, were identified as *Triatoma rubrofasciata*. Faecal material from the insects revealed the presence of a trypanosome which was proved, by inoculation of white mice to be *T conorrhini*. The same infection was found by xenodiagnosis in a live rat caught in a house infested with the infected bugs, although no trypanosomes were found in fresh blood preparations from the rat. In addition to trypanosomes in faecal material of bugs which had fed on the rat, typical trypanosomes were also found in the blood of mice infected by inoculation of such material.

*Trypanosoma conorrhini* was cultured readily on NNN medium from the blood of laboratory-infected mice and rats and from the naturally infected rat, even when direct examination of the blood was negative.

The author points out that as *Trypanoma rui* of seals and other *Trypanosoma* are frequently infected naturally with *Trypanosoma concolor*, this fact should be kept in mind, by those working on Chagas's disease, preferably when xenodiagnosis is being performed on wild or domestic animals, in the search for *Trypanosoma cruzi*. Laboratory animals should be inoculated with the flagellates found in the intestines of the bugs so that the blood parasites might be identified with certainty.

H J O D Burke-Gary

## LEISHMANIASIS

DORE, G. Maria. Contributo alla conoscenza della leishmaniosi in Sardegna. [Observations on Leishmaniasis in Sardinia.] *Pediatrics*. 1947 55 No. 13 108-15. [74 refs.] English summary (3 lines).

MOXIMET E. M. La leishmaniosi interna della Provincia di Palermo. Iulian; uno libro consideratur nella terapia. [Visceral Leishmaniasis in the Province of Palermo. Clinical Incidence and Observations on Treatment.] *Pediatrics*. 1940 July v 41 No. 7 465-9.

GRIDANI G. Sulla diffusione della leishmaniosi viscerale infantile nell'Arcipelago Toscano (8 casi osservati negli anni 1945-46). [Infantile Kala Azar in the Tuscan Archipelago. *Acta Med. Italica*. 1947 Oct. v 2, No. 10 300-33. 10 refs.] English summary (4 lines).

The author describes eight cases of infantile kala azar which he observed in the hospital of Portoferraio during 1945-6. Seven of these were from the Island of Elba and one from the Island of Pianosa.

C. M. Henon

GATTO I. Lo splenogramma nel kala-azar neonato. [The splenogram in Infantile Kala Azar. *Settimana Med.* 1940 Sept. 7 28 Year 34 n.s. v 2, Nos 38-39 105-12. 1 fig. [10 refs.]

The study of spleen smears from 28 cases of infantile kala azar has revealed the following cell types:

Haemohistioblastic cells divisible into indifferent haemohistioblasts and lymphoid or haematic haemohistioblasts; plasma cells mononuclear, divisible into histiocytoendocells, lymphoid and haemocyto-blastic cells; lymphocytic cells medullar cells divisible into granuloblastic and erythroblastic cells. The origin of these various cells from one original splenoblast is shown in the form of a tree. The variations in the occurrence are discussed and the changes undergone by them during treatment are noted. The differential count before and during treatment are given in two tables. The various cell types are illustrated in a series of photomicrograms.

C. M. Henon

MURARO G. La splenomegalia leishmaniosa nel quadro delle sindromi bantiene. [Leishmanial Splenomegaly in the Banti Syndrome.] *Pediatrics*. 1944-45 v 5, 53 1-52, 1 chart & 5 figs. 77 refs.]

In this article the author describes a fatal case of infantile kala azar in which the post mortem appearances showing curbing of the liver and spleen are suggestive of Banti's disease. He discusses various observations which have been made and concludes that leishmaniasis is one of the factors which may produce the Banti syndrome.

C. M. Henon

- MURANO, G Polipeptidemia ed azotemia nella leishmaniosi interna [Poly-peptidaemia and Azotaemia in Visceral Leishmaniasis] *Pediatrics* 1941 Dec v 49, No 12 636-53 [38 refs]

- CARNEVALE, A Sull'importanza dei fenomeni interferenziali nell'associazione lue-leishmaniosi [Syphills obstructing Treatment of Kala Azar] *Pediatrics* 1943, May, v 51, No 5, 145-55 [22 refs]

In describing four cases of infantile kala azar which resisted treatment with tartar emetic, the author noted that there was a concomitant syphilitic infection. Response to tartar emetic was only obtained after a course of treatment for syphilis had been completed. He considers that a syphilitic infection should be suspected in all cases of kala azar which resist antimony treatment.

C M Wenyon

- ROUMAGOUX, J Un cas de bouton d'Orient autochtone à Mecheria (Hauts-Plateaux oranais) [An Autochthonous Case of Oriental Sore in Mecheria] *Arch Inst Pasteur d'Algérie* 1947 Sept-Dec, v 25, Nos 3/4 196-8 [Refs in footnotes]

The first case reported from Mecheria Oran, at an altitude of 1 167 metres

See also p 447, NESS, BRADY, COWIE & LAWTON, Anomalous Distribution of Antimony in White Rats following the Administration of Tartar Emetic

## FEVERS OF THE TYPHUS GROUP

- ROY, H K & BHATTACHARJEE, R C Typhus Fever amongst the Civilian Population in Calcutta (With a Report of Three Fresh Cases) *Calcutta Med J* 1947 July & Aug v 44 Nos 7 & 8 164-5 190-94 3 charts

- MONTOYA, J A, OSEJO, P P & TOPPING, N H Typhus in Colombia a Survey of Four Towns by the Complement Fixation Test, November 1946 *Am J Trop Med* 1948, Jan, v 28, No 1, 163-71, 1 fig [10 refs]

The authors employed a complement-fixation test, in which *Rickettsia prowazekii* was used as the antigen, in a study of the sera of 966 persons between the ages of 5 and 49 years in four villages of South Colombia. The villages were about 3,000 metres above sea level, the average air temperature was about 11-12°C and the conditions of life were suitable in all respects for the maintenance of louse-borne typhus infection.

About 25 per cent of the sera gave positive reactions at titres of 1-8 or more and it was concluded that at least as great a percentage of the inhabitants had been attacked at some time with typhus fever.

The antigen used was not purified so as to differentiate between louse-borne and flea-borne typhus, but the epidemiological conditions described in the paper strongly suggest that the infection was louse-borne.

It is stated that there was no clear evidence that age or sex caused a statistically significant difference in the incidence of the disease, and that the incidence rates did not show peaks which could be considered as due to the occurrence of epidemics.

John W D Megaw

Kowicz, J. Techniques for Rickettsial and Virus Cultivation. *Proc. Soc. Exper Biol & Med* 1947 Oct., v. 68 No. 1 188-7

The technique described refers to the rearing of human body lice in sterile conditions for use in feeding experiments on patients suspected of being infected with virus and rickettsial diseases. Freshly hatched larvae, reared from eggs laid by laboratory bred lice which have to be fed twice daily on healthy persons, are fed on the patient in aseptic conditions twice daily for 4 to 12 days; the infecting organisms are sought in stained smears of the faeces and guts of the insects. Details of the technique are given.

The author states that he has "isolated and observed the infectious bodies responsible for a number of virus and rickettsiae-like diseases". The bodies are said to have been, for the most part round disks about the size of typhus rickettsiae and to have been causally associated with several diseases of a rheumatic type including acute rheumatism and chorea minor. In one case the disease was a toxic diarrhoea in an infant.

Larval bedbugs were reared in the same way and in some cases gave better results than louse larvae.

[It seems strange that the bodies seen in virus diseases should have been similar to those observed in rickettsial infections. The information supplied with regard to the practical application of the method of investigation is tantalizingly meagre. It is to be hoped that this aspect of the study will be dealt with in further communications.]

The early part of the investigation was carried out in the Weigl Typhus Institute at Lwow.] John W. D. Morgan

Giroud P. Pouvoir neutralisant de la streptomycine sur les Rickettsies du typhus épidémique mis en évidence dans la peau. [The Neutralising Effect of Streptomycin on Rickettsiae of Epidemic Typhus as shown by Skin Tests.] *C. R. Soc. Biol* 1947 Nov. v. 141 Nos. 21, 22, 1117-19 4 charts

The author studied the effect of streptomycin on rickettsiae of epidemic typhus by intranasal inoculation of mice and by skin tests on rabbits. In the former experiments, 20 anaesthetised mice received 6 drops of a rickettsial suspension and thereafter were given 2,000 units of streptomycin daily. In some cases, 10,000 units were injected on the first day. In a first series of experiments, no rickettsiae were found in the lungs of the treated mice. In a second series, rickettsiae were found in approximately equal degrees in lungs of treated and untreated mice alike. However in the case of the treated animals, the rickettsiae often stained less readily, took a blue instead of a red colour with Macchiavello's stain and were punctiform. In the control mice the morphology and staining of the rickettsiae were normal. Evidently the only action of the streptomycin on the rickettsiae was to modify their morphology.

In the skin tests, the skin of rabbits was inoculated with 1 mgm., 2 mgm. and 4 mgm. of lung tissue heavily infected with rickettsiae mixed with solutions of streptomycin containing from 1.8 units to 18,000 units. The suspensions and the dilutions of streptomycin were kept in contact for 1 hour at 30°C. Neutralization of the rickettsiae was assessed in terms of the delay or feebleness of the local reactions produced. A chart and a table in the text indicate that 1,800 and 18,000 units completely neutralized the rickettsiae up to the 4 mgm. quantities of infected tissue; the smaller doses had a correspondingly weaker effect and 1.8 units only neutralized 1 mgm. completely while 1.8 units had little effect.

The author concludes that streptomycin has a definite effect on typhus rickettsiae when tested intradermally, but this is less in evidence in the case of experimental pulmonary infection

H J O'D Burke-Gaffney

TUNA, I Yerli ve yabancı tífüs aşılarının muafiyet kudretlerinin karşılıklı mukayeseleri [Comparison between the Antigenic Power of Typhus Vaccines prepared in Turkey and elsewhere] *Türk İhtiyat Tecrübi Biyoloji Dergisi* Istanbul 1945, v 5, 107-14 [18 refs] French summary

In the author's laboratory at the Central Institute of Hygiene in Refik Saydam, typhus vaccine was prepared during the war by the cultivation of rickettsiae in the egg embryo (Cox). In the present investigation, the antigenic power of this vaccine was compared in guinea-pigs under carefully controlled conditions with vaccines from seven other prominent sources in Europe and the United States. The results are tabulated, and although not more than 10 guinea-pigs were used in any one test, it is claimed that the Refik Saydam vaccine was as active as the others, on the basis of the number of guinea-pigs successfully immunized with it

H J O'D Burke-Gaffney

COLE, L C & KOEPKE, Jean A Problems of Interpretation of the Data of Rodent-Ectoparasite Surveys and Studies of Rodent Ectoparasites in Honolulu, T H., Savannah, Ga., and Dothan, Ala *Supplement No 202 to Pub Health Rep* Wash 1947, 71 pp 3 figs & 3 maps [63 refs]

In the first part of this report, the authors discuss the complexities to be considered in applying the "flea-count" technique to investigations into the populations of rodent ectoparasites. The chief object of such surveys being to obtain an index from the raw data which will bear an approximate relationship to the total ectoparasite population sampled, it is essential that several factors which complicate such studies should be borne in mind.

Some of the points discussed include the accurate identification of species of ectoparasites and their hosts, their sex and age, food of the host, location of traps, number of traps, number of rats per trap, efficiency of the traps and of the trappers, and many more. The meaning and limitations of different types of indices are considered, in particular, the mean number of fleas per rat, mean *Xenopsylla cheopis* per rat, mean female *cheopis* per rat and corresponding indices for infested rats. The mean number of female *cheopis* per infested rat is probably the most promising of these indices for evaluating the effect of control measures, because normally it is the least variable, but the reader is warned that this index cannot yet be justified for use with other species.

It is pointed out that in different places, different factors may take precedence in influencing the index. The survival of fleas away from their hosts is promoted by low temperature and ample moisture, but a high temperature induces more frequent feeding and increases the proportion of males in the catches. However as the value of the vector-count technique seems to have been established it may perhaps merit extension into other fields of enquiry. For instance, it may be found that vector indices correlate more closely with enzootic typhus than with human typhus and more closely with the microclimate of the rat-holes than with data from weather stations, but these are subjects for special investigation and are not measurable from the data available in these reports.

The results of a survey of rodent-ectoparasites of Honolulu are then considered. Trapping of rodents began in January 1934 and ended in January 1935. Results for 282 days catches are analysed. Of 6 664 rats, 4,967 (74.5 per cent) were

*Rattus norvegicus* 1,238 (18.8 per cent.) were *R. rattus* and 459 (6.9 per cent.) were *R. argentensis*. The fleas from 6,382 of these rats numbered 41,400. *Echidnophaga gallinacea* formed over 59 per cent. and *Xenopsylla cheopis* over 39 per cent. other fleas taken were *Cimexopsylla felis* and *X. humanus*. The number of mites taken from 608 rats (a 10 per cent. sample) was 8,431 among them *Laelaps karstensis* accounted for over 91 per cent. *Echidnophaga echidnina* 8 per cent. and *Liponyssus bacoti* 0.4 per cent. Lice from the same 608 rats were 2,380 and of these *Polyplax spinulosa* amounted to over 82 per cent. and *H. papillipes* spp. to over 17 per cent.

The figures are analysed in a dozen tables and from these it is seen that *R. argentensis* had significantly fewer lice and fleas than *R. rattus* and the latter had fewer fleas than *R. norvegicus*. Mites occurred indiscriminately on the different rats. The mite *L. karstensis* was abundant in the wet season and the flea *X. cheopis* was most prevalent in the dry season. Certain aspects of these results seem to warrant further careful investigation, for the mite *L. karstensis* was apparently more abundant than the flea *X. cheopis* and the mite *L. bacoti* (a laboratory vector of rodent typhus) was comparatively rare moreover the survey shows that human incidence of typhus coincided more closely with the peak abundance of *L. karstensis* than with that of *X. cheopis*. These findings demonstrate the necessity for ectoparasite surveys in different places, at different times and under a variety of conditions.

The results of similar work in Savannah, Georgia, are next analysed in the same way except that all rats (rather than a 10 per cent. sample) are included in the examination for mites and lice as well as for fleas. Trapping was done from January 1932 to December 1933 during 617 trapping days. Here *R. norvegicus* formed over 90 per cent. of the total rat collection (7,813 rats) while less than 7 per cent. were *R. rattus*. The situation here appears to be even more complex because though Savannah is regarded as a city with a relatively high incidence of endemic typhus, this is not associated with any peculiar qualitative features disclosed by the analysis of the survey figures. The mite *L. bacoti* while more abundant here than in other cities surveyed (33,496 or 45 per cent.) failed to show the seasonal variations characteristic of this disease. The data for Savannah offer little information except that important ectoparasites were found. These were those named above with the addition of *Leptopsylla segnis* (a flea which was more closely associated with *R. rattus* than with *R. norvegicus*) and some other less abundant species.

The last part of the report deals with surveys at Dothan, Alabama, which is not a seaport. Rat collections were made from March 1933 to March 1934, during 317 trapping days. The figures analysed are those from 4,833 rats, of which *R. norvegicus* made up about 60 per cent. and *R. rattus* 0.7 per cent. Of 51,005 fleas *X. cheopis* accounted for over 48 per cent. *E. gallinacea* over 28 per cent. and *L. segnis* over 21 per cent. Of 15,251 mites, *E. echidnina* was easily the commonest, with over 91 per cent. and of the lice (8,900) over 93 per cent. were *Polyplax spinulosa*.

The results from the Dothan survey contrast with the results from other places. The area is one of high incidence of endemic typhus, and because of the low figures for *R. rattus* (45) and the mite *L. karstensis* (8) neither of which appear to be essential for transmission and because *P. spinulosa* and *E. gallinacea* though numerically adequate show variations inconsistent with typhus epidemiology suspicion is therefore directed to *X. cheopis*.

H. S. Llew

See also p. 423 WATSON RICHARD & TOULAC, Les rongeurs et insectivores de Léopoldville et leurs ectoparasites.



BERTAZZI, C G Ulteriore contributo alla terapia del dermatifo murino della Sicilia orientale mediante l'uso del chinino e della maretina [The Treatment of Murine Typhus in Sicily with Quinine and Marelina] *Acta Med Italica* 1947, Dec, v 2, No 12, 383-6 2 charts English summary

An account of two cases with apparently good results

WILEY, J S A Preliminary Report concerning DDT Dusting and Murine Typhus Fever in Nine South-eastern States *Pub Health Rep Wash* 1948, Jan 9, v 63, No 2, 41-3, 1 fig

In July, 1945, the U S Public Health Service inaugurated a typhus control programme in 9 south-eastern States, in collaboration with the State Health Departments The work was continued throughout 1946 and the first half of 1947 The programme involved primarily the application of 10 per cent DDT dust to rat runs, burrows and harbourages in an attempt to reduce rat fleas and other ectoparasites and so to control human murine typhus fever

This work was carried out in 122 of the highest typhus reporting counties in the 9 States, which between them had accounted in 1944 for 72.3 per cent of all typhus reported in these "typhus" States or 70.5 per cent of all typhus reported in the entire U S A

A table and a figure show the results of these dusting operations, tabulating separately the figures from the 122 counties which operated the dusting projects and those from the 460 counties which did not The year 1944 is also shown as a "precontrol" year

These results show that in the period July-December 1945 a decrease in reported typhus of 10.7 per cent occurred in dusted counties compared to an increase of 14.5 per cent in the non-dusted counties, a differential of 25.2 per cent In 1946 and half of 1947 the differentials were 44.1 per cent and 56.4 per cent

The reported cases decreased in the 10 highest "typhus" counties from 1,074 in 1944 to 395 in 1946 In tabulating the results, DDT dusting is the only control measure taken into account

In the treated areas, flea counts from some 17,000 live rats have indicated that *X. cheopis* reduction has averaged 84 per cent

H J O'D Burke-Gaffney

BETTINARDI, G La febbre esantematica mediterranea [Mediterranean Exanthematic Fever] *Pediatria* 1942, Sept, v 50, No 9, 343-52

The author presents a critical summary of the extensive literature connected with the tick-borne typhus fever which occurs in the countries round the Mediterranean Sea, and which has been described under such names as bouton-neuse fever, escharo nodular fever, eruptive Mediterranean fever, Carducci's disease, benign "non-diffusible" dermo-typhus Marseilles fever, etc

The paper contains much information that will be found useful by students of the typhus fevers though some of the author's statements may be misleading to the uninitiated reader, for example, flea-borne typhus is constantly referred to as Brill's disease Stress is rightly laid on the doubt that exists as to whether all the cases described as belonging to the Mediterranean exanthematic fever sub-group have been correctly diagnosed, neither the Weil-Felix reaction nor the response of guinea-pigs to inoculation can always be relied on to differentiate the disease from murine typhus

In clinical diagnosis special importance is attached to the rash, which in most cases appears between the 2nd and 4th day, and when fully developed consists

of discrete papules, or even nodules (and tends to be widely distributed) extending to the face, palms and soles. Constanzi is quoted as saying that an eschar occurs in 30 per cent. of the cases.

John W. D. Meigs

PHILIP C. B. Comments on the Name of the Q Fever Organism. *Pub. Health Rep. Wash.* 1948 Jan. 9 v. 63 No. 2 58.

In this brief note the author produces arguments to support the use of the name *Coxiella* for the aetiological agent of Q fever *R. burnetii*. He has been using the name as a full genus for teaching and other purposes during the war. "It is here proposed to validate that usage by elevating *Coxiella* to the status of a full genus the genotype, of course, remaining the same i.e. *R. burnetii* Derrick, which now becomes *Coxiella burnetii* (Derrick)".

H. J. O'D. Burke-Gaffney

SMADAL, J. E., SNYDER M. J. & ROBBINS, F. C. Vaccination against Q Fever. *Amer. J. Hyg.* 1948 Jan., v. 47 No. 1 71-81 1 fig. [22 refs.]

The authors working at the U.S. Army Medical Centre at Washington, D.C., prepared vaccines from yolk sac cultures of an Italian (Henterling) and an American (Dyer) strain of *Rickettsia burnetii*. A concise description is given of the methods employed in preparing and testing the vaccines.

Guinea pigs inoculated with either of the strains of vaccine showed a rapid rise in the complement fixation titre for the Italian strain of antigen, starting about two weeks after inoculation but the rise in the titre for the American strain of antigen did not occur till about four weeks after inoculation. After about eight weeks the titres for both strains of antigen were approximately equal.

Guinea pigs that were already positive for the Italian strain, but had not become positive for the American strain, appeared to have acquired the same high degree of relative immunity against both strains of infection as was shown by the guinea pigs positive for both strains of antigen.

Among 28 volunteers inoculated with the Italian strain of vaccine 23 gave complement fixation titres of 1:20 or more when tested two weeks later with Italian antigen but all were negative to tests with American antigen.

Among 11 volunteers inoculated with the American strain of vaccine seven reacted at 1:20 or more to tests with the Italian antigen but only one reacted with the American antigen.

By later tests it was found that few of the volunteers ever developed complement fixing antibodies for the American strain and that only two failed to develop antibodies for the Italian strain though in a few cases the titres were only 1:5 or 1:10.

There was no opportunity for testing the efficacy of the vaccines against human infection.

John W. D. Meigs

## YELLOW FEVER

KIRK, R. Eradication of *Aedes aegypti* in Khartoum. [Correspondence.] *Nature*. 1948 Jan. 24 139.

The author writing from the Stack Medical Research Laboratories Khartoum, refers to an editorial note in *Nature* 1947 August 9th 188 in which it is stated that yellow fever has been eradicated from Khartoum "result of mosquito control measures". He points out that while *Aedes aegypti* has been

virtually eliminated in Khartoum, there is in fact no evidence of actual yellow fever infection ever having been identified there. Khartoum is north of the local yellow fever endemic area and immunity surveys show no evidence of infection having occurred during the life-time of the present inhabitants.

Since the successful anti-mosquito campaigns of BALFOUR some forty years ago, the mosquito situation in Khartoum has been observed constantly records over that period suggest that *A. aegypti* has never been very abundant in that desert neighbourhood and has been eradicated, to reappear infrequently and be rapidly destroyed. Such reappearances in the past were probably re-importations, since the mosquito at one time was regularly brought to Khartoum by river steamers but the great reduction of mosquitoes on steamers is one of the effects of the present mosquito control measures in the Sudan described by LEWIS [this *Bulletin*, 1947, v 44, 656] whose paper was the subject of the editorial note referred to above. *A. aegypti* has not been reported on those steamers for several years.

H J O'D Burke-Gaffney

## PLAGUE

WANSON, M, RICHARD, P & TOUBAC, M. Les rongeurs et insectivores de Léopoldville et leurs ectoparasites [Rodents and Insectivores of Leopoldville and their Ectoparasites] *Rec Travaux Sci Méd Congo Belge* 1947, July, No 6, 3-38, 8 figs, 1 chart & 24 photos [50 refs]

A list is given of the names of 7 species of *Insectivora* and 26 *Rodentia* found in the Léopoldville area of the Belgian Congo. Among 29,245 domestic rodents examined, no specimen of the brown rat (*Rattus norvegicus*) was seen, but there were four forms of the black rat, namely *R. rattus* (1,772), *R. alexandrinus* (14,607), *R. frugivorus* (12,854) and *R. wroughtoni* (112). Among 10,461 non-domestic rodents taken outside the town, 22 species were represented, the commonest being the marsh rat *Dasymys benileyae* (5,689).

Descriptions are given of the animals, their burrows and their nests and a key is provided for their identification. There are also drawings and photographs of certain diagnostic characters, but, unfortunately, some of the names under the photographs of skulls have been misplaced and it has been necessary to insert a correction sheet in the volume.

Among the fleas taken from the domestic rodents, *Xenopsylla brasiliensis* was most common, being taken 29,008 times, *X. cheopis* was collected 13,816 times, *Ctenocephalides felis strongylus* 242 and *Echinophaga gallinacea* 158 times, maximum numbers were collected in the cool, dry months of August and September. The two species of *Xenopsylla*, though abundant on the rats, were rarely seen in houses. In African huts, *C. felis strongylus* and *Tunga penetrans* were common. *Polyplax spinulosa* was the only louse on the four black rats, though no numbers are given. In the dry season, the mites *Dermanyssus muris* and *Liponyssus bacoti* appeared on *R. alexandrinus*, from 600 rats, 210 *L. bacoti* were taken, the first time this mite has been identified from the Congo. Species of *Laelaps* also occurred, but only averaged 8 mites per 1,000 rats. Nymphs and adults of the tick *Haemaphysalis leachi* were collected but the numbers are not stated.

On 10,409 field and woodland rodents, 80 per cent carried mites, 1 per cent fleas and 19 per cent were free of ectoparasites. The fleas were *X. nubicus*, *X. brasiliensis* and *X. cheopis*, fleas of other genera were absent. Mites of the genus *Laelaps* were common, especially on some specimens of the marsh rat (*D. benileyae*), which were free of fleas. A few *H. leachi* were obtained and

some *Rhipicephalus simus* and *R. sanguineus*. At the mouth of the berru  
*Phlebotomus schweileri* *P. africanus* *Mansonioides africanus* *M. uniformis* and  
*Culex fatiga* were taken on oiled paper traps. H. S. Linton

ERZIN N. & PATEV S. Akçakale vebasi. (Plague in Akçakale) *Türk İhtiyat Tercümesi Brivoloji Dergisi* Ankara. 1947 1 7 No 3, 31-44. figs. & 1 folding chart. English summary

In March-April 1947 19 cases of plague occurred in Akçakale Turkey 14 were axillary bubonic and 5 were septicæmic. Plague serum from the Pasteur Institute (80 cc daily) was not satisfactory but sulphadiazines proved of great value in treatment. In some cases these drugs were combined with serum therapy.

Serum and sulphadiazine were given prophylactically to 8 relatives of patients; they did not develop the disease but four persons who refused this treatment developed typical bubonic plague. As an insecticide 6 per cent. DDT in petrol was very satisfactory. H. J. O'D. Burke-Jones

FALST E. C. Plague in the Americas. *Leder J. bilisus J. Radhain* (San. Beg. *Med Trop. Brunsd*) 1947 Dec. 113-14 2 figs. (maps). [17 refs.]

Plague in the Americas has been well reviewed in a large number of publications and the history of its introduction to the American continent in 1899 by the Dutch ship *Zur* should be well known. In this article there is reference to the accepted view of how plague became established in ground squirrels. The San Francisco disaster of 1906 resulted in the escape of city rats from the Chinese shums into the hills and the transference of their fleas to the squirrels. In continuation of this explanation there comes the author's view that it can never be proved that this so-called Asiatic plague did not exist prior to the San Francisco earthquake and even before the introduction of rat plague from China. Could this be comparable to the existence of endemic plague in the human hills of British India before its arrival at Bombay from Hong Kong. The author considers that plague exclusively in domestic rats could be eradicated but that the danger remains of reintroduction to the rat population of the infection from the enzootic plague of wild rodents. His views on the transmission of plague in South America may be contested. But he says that if the domestic rat was the original reservoir among these people it has ceased to be important for the disease is to-day transmitted by human rather than rodent ectoparasites—that is to say by the human flea or ear louse and from man to man. W. F. Harris

## CHOLERA

BIRALD Y. & KALL P. M. World Distribution and Prevalence of Cholera in Recent Years. *Epidemiological & Social Statistics Rep. W.H.O. International Commission* 1947 Dec. 1 No. 7 140-34 3 charts & 1 map. In parallel French & English

This document on the recent cholera epidemic in Egypt is of great importance, as it does from the World Health Organization of the United Nations. In its explanation of the origin of the epidemic it follows standard and regulation lines. If that explanation is not wholly acceptable it simply means that ignorance still prevails on the subject of cholera—not so much perhaps on its epidemiology as on its endemology.

The epidemic was unexpected, and it is stated categorically that, 'Cholera still fully deserves its qualification of "Asiatic" because for the last thirty years it has been confined to that continent' There is abundant evidence that India is the most persistently affected part of Asia, but we learn that figures for British India are more reliable than elsewhere and that British India up to 1947 contained some three-fourths of the population of India Prominence of the cholera of British India may have something to do with the reliability of its statistics By British India is meant, for the most part, the Gangetic Valley and the city of Calcutta, although in the present case attention is directed rather to the Punjab Particular note is taken in this publication of those correlated factors in epidemic cholera —famine, war, pilgrimages and panic-stricken populations In India, the Japanese war menace, the Bengal famine and the large-scale movement of population as a result of partition are rightly noted

The earliest history of the present epidemic is very interesting, because "the first three cases were believed to be food poisoning," that is to say, presumably, something more severe than subclinical cholera or mild diarrhoea A very important factor in the subsequent development of the epidemic was that El Koreim, the focal point, was overcrowded with a non-resident population a stampede of this population spread the epidemic first over the lower Nile provinces and then over the upper Large cities with a chlorinated water supply and satisfactory sanitation escaped very lightly, as one may expect is the position of Europe to day compared with last century

Some note may be taken of the record that "the source of the epidemic is still obscure" and that "first-hand observers think they can trace the origin of the infection to Egyptian labourers infected by aeroplanes coming from India' The explanation offered seems to be that of the landing of a germ carrier from India There is positive evidence that cholera was absent during the Mecca pilgrimage in 1947 and that the epidemic broke out before the return of the pilgrims

A contention that vaccination of the whole population and the winter season, unfavourable to cholera prevalence, both played their part in the limitation of the outbreak might perhaps be met by opposing the remarkably similar graphs of cholera epidemic for 1902 and 1947 No vaccination can have been instituted in 1902 The longer duration of the epidemic in 1896 might reasonably be given as being due to the season of its occurrence, May to October We may note also the intention of the authorities to institute a vaccination campaign to cover the entire population in 1948 Practically no mention is made in this account of chemotherapy for cholera, among the highly commendable and energetic activities of the Egyptian authorities

IV F Harvey

GALLUT J & GRABAR P Recherches immunochimiques sur le vibron cholérique V Absence de pouvoir antigénique de la substance hypothermisante de la toxine cholérique [Absence of Antigenic Power in the Hypothermy-producing Component of Cholera Toxin] *Ann Inst Pasteur* 1947, Nov, v 73, No 11, 1139-42

Two different fractions are demonstrable in cholera toxin, one of large molecule ( $d > 100 \mu\mu$ ), a conjugate protein of glucolipidic type, and another of small molecule ( $d < 4 \mu\mu$ ) of unknown character, but causing hypothermy [this *Bulletin* 1943, v 40 910, 1944, v 41, 401 and 402, 1945 v 42, 807 1946, v 43, 129] The first component is identified as cholera O antigen and, as an antigen, furnishes a neutralizing antiserum This antiserum has no action on the second component The present research sets out to determine whether

the second component is antigenic and to investigate its specificity. The authors find that it is devoid of antigenic power.

W. F. Harvey

## AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

REES C. W. & REARDON Lucy V. Problems on the Growth Requirements of the Parasitic Protozoa. *Liber Jubilare J. Rodhain* (Soc. Belg. M. Trop. Brussels) 1947 Dec. 303-35. [80 refs.]

This paper is a review of literature dealing with the cultivation of *E. histolytica*, various Trichomonadidae, pathogenic trypanosomes and leishmanias and poecas of *Plasmodium* with particular reference to the constituents of the media employed. The various papers referred to have been reviewed in this Bulletin.

C. M. Wrenyon

SPRINGARN C. L. & EDLMAN M. H. The Prolongation of the Viability of Cultures of *E. histolytica* by the addition of Streptomycin. *J. Parasitology* 1947 Oct. 1, 33 No. 5 416-18.

The authors have found that cultures of *Entamoeba histolytica* on Dilco amoeba medium covered with horse-serum saline and having rice particles added progress satisfactorily when subculture is made every 48 hours. Act amoebae can be found in these cultures up to the 8th day. After the addition of 1 (XX) 3 (XX) units of streptomycin to the serum saline amoebae grew in rare instances but after 24 to 48 hours the amoebae were fewer than in the controls, though they appeared to be normal in size and motility and in their power to ingest rice. The average survival time in streptomycin cultures was 33.7 days in contrast to 8.0 days in controls. Some cultures survived 40 or 50 days and one 70 days. In the streptomycin tubes bacterial growth was markedly inhibited.

C. M. Wrenyon

WRIGHT A. W. & COOMBS A. E. R. Treatment of Amoebic Dysentery. *Lancet* 1948, Feb. 14 743-6 3 figs. 20 refs.

Not only was the incidence of amoebic infection in India Command down to that of the average pre-war rate but response to treatment was poor.

The importance of early diagnosis became clear. On the day after admission sigmoidoscopy was done as a routine. A warm stage and warm saline were used and material from rectal or sigmoid swab was immediately examined under the microscope.

Esmine bismuth sulide was frequently given in tablets. In three patients it was ascertained by radiography that they were not being absorbed. These cases and a number of others similarly treated showed no grey discoloration of the stools, such as is seen after proper administration of E.H.I. Early in the investigation it became apparent that though fresh cases responded well to thorough course of treatment the relapsing cases and those with a long history before treatment did not. A further important factor appeared to be a secondary bacterial infection. Isolation of a pathogenic organism or the finding of a bacillary exudate was taken as evidence of such an infection which was proved in 41 per cent of cases. The incidence was not significantly greater in chronic than in fresh cases. On these premises course of treatment was devised.

consisting of 2 mega units of penicillin and 65 gm succinyl sulphathiazole followed by E B I and quinoxyl enemata for 12 days and carbarsone for 10. In all, 92 patients were given penicillin. Sigmoidoscopy was carried out before and after this treatment and in every case where ulceration had been seen there was striking improvement.

On the completion of treatment, the patient was retained in hospital for ten days, during which 6 stools were examined and sigmoidoscopy was done. After a period of three weeks in a convalescent depot, he returned to hospital for a week. Three more stools were examined and sigmoidoscopy was repeated. If he was apparently cured, he was discharged and required to report by postcard in three months' time. The importance of sigmoidoscopy is emphasized, as lesions suggesting amoebiasis were present in 88 per cent of cases with negative *E. histolytica*.

In 21 per cent of cases, the organisms were present in the swab when the stool was negative.

Cure was effected in 97.5 per cent of primary cases with symptoms lasting two months or less, 96.1 per cent of all primary cases were cured, 85 per cent of those with one previous attack, and only 58.4 per cent of those with more than one attack.

P. Manson-Bahr

MANSON-BAHR, P. & MUGGLETON, W. J. The Response of Intestinal Amoebiasis to Diodoquin Treatment. *J. Trop. Med. & Hyg.* 1948, Feb. v 51, No 2, 23-7 [10 refs.]

The authors treated 71 patients suffering from intestinal *Entamoeba histolytica* infections with Diodoquin (Searle). The dosage was two tablets (6.4 grains) four times daily after food for fifteen days. The patients could be divided into four groups as follows—

**Series I**—Six with acute amoebic dysentery. The drug proved valueless in these.

**Series II**—Twelve with a history of amoebic dysentery in the preceding five years but quiescent at the time of treatment. One had an acute clinical relapse within three weeks, eleven were free from cysts three to sixteen weeks after treatment.

**Series III**—Twenty-three with a history of previous diarrhoea. One continued to pass cysts throughout and after treatment, twenty-two were free from cysts three to 104 weeks after treatment.

**Series IV**—Thirty apparently healthy carriers with no history of diarrhoea. All were free from cysts three to 120 weeks after treatment. [Six was the maximum number of stools examined in any one case of the four series.]

There was no evidence of genuine toxic action of the drug in the 71 cases. Sigmoidoscopy or proctoscopy, where these were done, showed typical amoebic ulceration in the Series I cases, a pigskin type of pitting in the Series II and III cases and a normal mucosa in the Series IV cases.

The nature of the infection in the carrier, or symptomless cyst-passer state, is discussed. The authors incline to the view that *E. histolytica* lives in the lumen of the bowel as a coprozoic organism in some cases. This type of infection is eradicated by diodoquin, which is an efficient drug for this purpose as it is dispersed in the intestine and is not absorbed to any material extent. Cysts of non-pathogenic amoebae, and of *Giardia intestinalis* when these were present, disappeared after diodoquin treatment but the latter reappeared within two months.

J. R. D. Adams

Coxam N. J., Jr. Chloroquine in Amebiasis. *Amer J Trop Med.* 1948 Jan. v 28 No. 1 107-10.

In view of the occasional toxicity of emetine, it is desirable to have a safe and non-toxic substitute for it in the treatment of amoebic involvement of the liver. Some members of the 4-aminoquinoline series, which have a high antimalarial activity can be given in a non-toxic dosage which is associated with localization in high concentration in tissues especially the liver.

The author studied the anti amoebic activity of one of these compounds, chloroquine (see this *Bulletin* 1948, v 45 37). He quotes the work of BERLINER *et al.* (in the press) indicating that this drug is localized in the liver of the rat in concentrations 400 to 600 times those in the plasma.

A table shows that *in vitro* chloroquine had an amoebicidal activity greater than that of Anayoden and Carbarsone but less than that of emetine. In human amoebiasis, chloroquine was given firstly as a priming dose to saturate the tissues and rapidly obtain the equilibrium plasma concentration and secondly as sustaining doses for 2 or 3 weeks. The doses used were far in excess of those required for antimalarial activity and were about one-half of the believed minimal toxic dose, as estimated by Berliner *et al.* The priming doses consisted of 0.3 gm. of the base twice daily for 2 days and the sustaining doses were 0.3 gm. daily for 12 or 16 days more. All doses were given orally.

In these experiments plasma concentrations of the drug were not determined but from the work quoted above it is indicated that they would amount to about 150 microgrammes per litre. No toxic symptoms were observed, but two patients with amoebic hepatitis had mild and transient gastric symptoms. Altogether 28 patients with intestinal amoebiasis and 8 with amoebic hepatitis were treated with Chloroquine. Thirteen of the former continued to show parasites in the stools after one course of treatment the other 15 have had persistently negative stools for 2 to 8 months. The author emphasizes that as the follow-up period lengthens the figures can only change unfavourably.

In the 6 cases of amoebic hepatitis, symptoms and signs disappeared sharply within a few days of the beginning of treatment they have not recurred within 2 to 4 months.

The drug had no effect on non-pathogenic intestinal protozoa or on a number of species of helminths.

As chloroquine is almost entirely absorbed from the gastro-intestinal tract, its effect on amoebae in the colon must be due to plasma or tissue concentration.

The author states that this report is wholly preliminary and its primary purpose is to call attention to the anti-amoebic activity of this non-toxic drug and to encourage others to test it especially in amoebic hepatitis.

H. J. O'D. Burke-Gaffney

FELTON J. D. & JOYNER L. P. Natural Amoebic Infections in Laboratory Rodents. *Nature* 1948 Jan. 10 68-8 6 figs. 710 refs.

In the course of chemotherapeutic work on *E. histolytica* the following animals were examined for naturally occurring amoebic infections—white rat, cotton rat (*Sigmodon hispidus*), hamster (*Cricetus auratus*), Orkney vole (*Microtus oeconomus*). In all of these an amoeba resembling *Entamoeba* was discovered in 50-100 per cent of animals examined. The amoebae and their binucleate cysts are illustrated in microphotographs. Attempts at cultivation of the amoebae failed.

C. M. Henry



## RELAPSING FEVER AND OTHER SPIROCHAETOSSES

GAUD, M & MORGAN, M T Epidemiological Study of Relapsing Fever in North Africa (1943-1945) *Bull World Health Organization* (United Nations) 1947/48, v 1, No 1, 69-92, 1 map & 2 charts

An U.N.R.R.A. Mission consisting of Dr Gaud and Dr Morgan proceeded to French North Africa in November 1945 in order to study the epidemic of louse-borne relapsing fever which, after 25 years' quiescence, had spread rapidly through Tunisia, Algeria and Morocco. The last epidemics were in North Africa between 1912 and 1915 and in French West Africa between 1922 and 1925. During the intervening period, only small foci of the tick-borne disease existed.

This study is divided into three parts: epidemiological, clinical and therapeutic. It was shown that the origin of the epidemic was in the Fezzan region of southern Tripolitania. This was also thought to be the reservoir of the virus in the 1912 epidemic by NICOLLE (whom the authors frequently quote and whose work permeates the whole story of relapsing fever). The disease apparently began in the nomad tribe of Megarha in the last quarter of 1942. Caravans spread the disease throughout the Fezzan and half the population became infected between November 1942 and May 1944 when the infection died out. The neighbouring countries, however, passed on the infection, which eventually reached Morocco in the west. In Tunisia, approximately 400,000 cases occurred (20 per cent of the population); in Algeria, 432,000 (5 per cent of the population); in Morocco, perhaps 180,000 cases.

The epidemic was associated with a grave economic crisis, which has long been recognized as an essential precursor of louse-borne epidemics. Contrary to the classical notion that cases should be most numerous in the winter, on this occasion, there was no seasonal trend and the epidemics developed rapidly, irrespective of the season of their inception.

No actual evidence is cited that the louse was the vector of the disease in North Africa, though it was assumed to be so. The role of the bed bug was investigated and work at the Casablanca Pasteur Institute has shown that these insects can become infected by biting an infected person and that they are still infective after the first moult, as can be proved if they are crushed and injected.

The use of DDT has revolutionized the methods of control and the systematic use of this insecticide has proved completely efficacious. The inhabitants welcome this method which they recognize as valuable and harmless. Unfortunately, supplies of this substance do not appear to have been adequate and there is no mention of its widespread use. In fact the history of the epidemic itself shows the lack of effective control.

The clinical features were varied and every organic system was affected. Headache was always violent, and accompanied by bilious vomiting and pain in the joints. There was usually only one relapse, which ensued after a week's apyrexia. The most frequent complications were hepato-nephritis and peripheral haemorrhages. Neurological forms occurred, especially pseudo-meningeal conditions and various psychoses. Ophthalmic complications were numerous. Some of these were associated with the ipecic therapy. Premature termination of pregnancy was virtually inevitable and this is ascribed to the death of the ovum after an enormous drop in the proteins in the maternal blood, which leads to dehydration and cachexia.

Mortality figures cannot be assessed accurately, but apparently varied in hospital cases from 3.6 per cent in the well-to-do to 87 per cent in the poverty-stricken. In the untreated, the figure varied between 5 and 10 per cent.

Different spirochaetocidal drugs were employed—antimony bismuth and mercury salts were relatively inefficacious. Pentavalent arsenic was successful in curing the infection, but was sometimes followed by ocular disasters. The best drugs were the less toxic trivalent compounds (Neocarsphenamine, Maplasen). The standard course of the former was 0.3 gm. the first day, 0.45 gm. the second and 0.6 gm. the fourth. An interesting new method was employed on 32 cases, namely treatment with convalescent serum (30 cc. intravenously) 80 per cent. of the patients so treated were cured in 12 hours.

The authors conclude by stating that the immense region along the South Coast of the Mediterranean is the real sanitary frontier of Europe, a frontier easily crossed because the Mediterranean is a sea which unites rather than divides—beyond this frontier all the major epidemic diseases are rampant.

P. C. C. GARDNER

GAUD M. KHALIL Bey M. & VALCEL, M. The Evolution of the Epidemic of Relapsing Fever 1942-1946. *Bull. World Health Organization* (United Nations) 1947/48, v. 1 No. 1 83-101

This paper forms a corollary to the one abstracted above (GARDNER) and describes the extension of the epidemic throughout North Africa and the Middle East. The chronology of the disease in the larger field appeared to be as follows—

Last quarter of 1942	Fezan, S. Tripolitania
October 1943	Tunisia
November 1944	Algeria
Early 1945	Morocco
November 1945	Tangier
1945	Egypt
1945	Kenya
February to June 1945	Iran

The epidemic traversed the whole of North-West Africa like a storm. Eastwards the disease was first recognized at Asut in October 1944 but this threat to Egypt did not materialize until the following year, during which and in the first half of 1945 over 100,000 cases were reported, the peak notifications being in April 1946. Throughout 1945 and 1946 small numbers of cases occurred in the Middle East including Transjordan, Palestine Syria, Iraq and Aden. The disease attained epidemic proportions in Kenya and Iran.

The threat to French West Africa was partly averted by the institution of strict sanitary measures at Dakar on the arrival of convicts, but there is nothing to prevent the importation of the disease by land and the danger of this country remains great.

Relapsing fever in epidemic form in Europe was confined to Rumania, where over 5,000 cases occurred in the first six months of 1945. It is unknown whether there is an aetiological connexion between this focus and the outbreak in North Africa.

The epidemic started as a few cases in a semi-desert region, progressively invaded the whole of North Africa from the Atlantic to the Red Sea, and is now threatening Central Africa and Europe.

P. C. C. GARDNER

SALLÉ, L. La fièvre récurrente à Fes (1945-1946). *Relapsing Fever in Fes*. *Cahiers Médicaux de Fes*, 1947 June, No. 11 431-7

The author states that the infection seems to have been brought into Fes by agricultural workers from the Oujda area in May 1945. The number 1

cases reached a maximum in September, since when it has persisted at a somewhat lower level. Lice, and "probably" bugs, are considered to be the carriers [There is no evidence in support of this statement] The author observed and treated more than 1,000 cases during eight months ending January, 1946

The incubation is said to be very short, only 2 or 3 days, and the author states that he was bitten by a louse on Wednesday at 8 p.m., and developed a febrile attack on Saturday at 2 p.m. A few observations are given on the clinical symptoms of the patients. The treatment adopted was acetylarsan, during the first 48 hours, and Mapharsen or Fontarsan when the infection was at its height

E Hindle

BODMAN, R. I. & STEWART, I. S. Louse-borne Relapsing Fever in Persia. *Brit Med J* 1948, Feb 14, 291-3, 2 charts [14 refs]

Between November, 1945, and June, 1946, an epidemic of louse-borne relapsing fever occurred in Abadan, 1,087 cases being admitted to the isolation hospital. The authors have found no report in the literature of louse-borne relapsing fever in Persia, but the present epidemic was undoubtedly part of the widespread epidemics in the Mediterranean and North Africa during 1943-45. The epidemic closely followed the cold weather, and quickly declined as the general temperature began to rise. Charts comparing this outbreak with a typhus epidemic in Abadan in 1943 show a striking similarity in the critical temperatures for the termination of the epidemics.

The diagnosis of louse-borne infection was based on the following points: (1) No tick focus has been found in Abadan and it is believed that no human ticks occur there. (2) Lice were found to have infested 88 per cent of the patients admitted to the isolation hospital. (3) *Trep. recurrentis* was found in lice taken from the patients. (4) The epidemiological features were characteristic. (5) Mass disinfection with DDT powder caused a drop in the weekly admissions.

Special clinical examinations were made of the last 214 cases admitted. Most of these patients were young adult males of the labouring and unemployed classes. The symptomatology is described. A point of interest was the frequency with which patients could fix the time of onset which was ushered in with a splitting frontal headache. The period of apyrexia lasted about 9 days, although the most constant time-relationship was from onset to relapse, which averaged 14 days. Rashes were rarely seen, in those few patients having a petechial rash on the trunk, the Weil-Felix reaction showed only a slight *Proteus OXK* agglutination (e.g.,  $1/25+$ ,  $1/50\pm$ ). Jaundice was not uncommon in 9 cases it was marked, and this was a bad prognostic sign—two of such patients died. The spleen showed all degrees of enlargement. The percentage incidence of symptoms and of signs is shown in tabular form and the authors note that the central nervous system is predominantly affected. 90 per cent of their patients complained of headache and 77 per cent of backache in the thoracic and upper lumbar regions. Two patients had mental derangement and there was one case of transverse myelitis. These last three were however the only complications seen in the central nervous system. Respiratory complications were the commonest amounting to 60 per cent. They varied from 'cough' to bronchopneumonia. The overall death rate amounted to 1.11 per cent.

The 214 cases specially studied were treated in two groups. Group I (97 patients) were given 0.45 gm. NAB intravenously on admission. 11 patients relapsed once. In group II (117 cases) the dose was not given until the case

relapsed, which occurred in 73 cases. This saved the drug, which was short at the time and also demonstrated its effectiveness in group I.

Few reactions followed the injection of VAB—no definite time interval was noticed between the injection and the crisis.

Of the nine patients with marked jaundice three were not given VAB on admission owing to the liver damage already present. Two of these three died. The remaining six received VAB on admission and none of them died.

H. J. O'D. Burke-Gaffney

BALTAZARD M. BAHMANYAR, M. & MOFII C. *Fébriles récurrentes transmises à la fois par ornithodores et par poux.* [Relapsing Fevers transmitted both by *Ornithodoros* and Lice.] *Ann. Inst. Pasteur* 1947 Nov v 73 No 11 1006-71

The authors have shown the resemblance between *Spirochaeta* *littoralis* and certain strains of spirochaetes occurring in rodents and *Ornithodoros* (see this Bulletin 1947 v 44 906).

In a first series of experiments, various batches of *Ornithodoros erraticus* *O. lahorensis* *O. turicata* and *O. parkeri* were fed on newly born rabbits heavily infected with *S. eruntensis* and subsequently tested for infectivity with uniformly negative results.

In a second series human lice were fed on newly born rabbits infected respectively with a strain of *S. maritima* from *O. erraticus* obtained in Persia, and *S. turicatae* and *S. hermsi* both North American strains isolated from *O. turicata* and *O. hermsi* respectively. The lice were fed once on a heavily infected rabbit and subsequently maintained on a human subject. After intervals ranging from 9 to 12 days the lice were ground up and inoculated into newly born rabbits. In every case these became infected, showing that these naturally occurring rodent strains although normally transmitted only by ticks belonging to the genus *Ornithodor* are also capable of survival in the human body louse. E. H. Adle

WOLSTENHOLME B. & GEAR, J. H. S. *A Complement Fixation Test for the Diagnosis of Relapsing Fever.* *Trans. Roy. Soc. Trop. Med. & Hyg.* 1948 Jan v 41 No 4 313-17

It is notoriously difficult to find *T. p. dubius* in many chronic infections of relapsing fever during the afebrile intervals. The authors have therefore devised a complement fixation test as an additional diagnostic aid.

The antigen is prepared by establishing *T. p. dubius* in egg-culture. This is achieved by inoculating eight fertile eggs on the 7th day of incubation, through the blunt air sac end with 0.4 cc. of heart blood from an experimentally infected mouse. After a week incubation at 37°C. the eggs are opened, and the blood-essels of the chorio-allantoic membrane are torn and allowed to bleed into the allantoic fluid. This mixture serves as an inoculum (0.1 cc.) for further batches of eggs, the trays from which, in the authors' case have been subcultured for ten weekly passages with somewhat variable growth of spirochaetes.

A sample of the blood-allantoic fluid mixture is examined by dark ground and stained smears, and it is only used if the degree of infection is profuse (e.g. 50 to 100 spirochaetes per field). The harvested fluid is centrifuged at 1,000 r.p.m. for 5 minutes, and the supernatant then centrifuged for 3 hours at 7,000 r.p.m. The resulting white sediment represent the spirochaetes, and the supernatant allantoic fluid is now replaced with 0.3 per cent sterile phenol saline. When this is shaken an even suspension is obtained and this constitutes antigen.

its anti-complementary properties were found to be low and it could be used undiluted [For detailed steps in the egg-culture and preparation of the antigen, the original paper should be consulted.]

For the test, the sera were inactivated at 56°C for 30 minutes and serial dilutions were made from 1/12.5 to 1/100 and thereafter to 1/3,200

Tubes corresponding to each dilution were set up and to each was added 0.1 cc of the appropriate serum dilution and 0.1 cc each of 3 M H D guinea-pig complement and of undiluted antigen. One extra tube was used as an anti-complementary control and contained 0.1 cc of normal saline instead of antigen. The tubes were placed in a 37°C water bath for one hour, when fixation took place. To each tube, 0.1 cc of 3 per cent washed sheep cells, sensitized with 6 M H D of amboceptor, was added and the tubes were incubated at 37°C for a further 30 minutes, after which the results were read.

A table shows the results of the test in 6 confirmed cases of relapsing fever. All gave a positive result in a titre of 1/25 and five of the six were + or ± at 1/100.

Twenty-four sera sent for routine blood grouping were negative, of thirty sera giving a strongly positive Wassermann reaction, one was anti-complementary in the present test, 4 gave a ± result at 1/12.5 and the remaining 25 were negative. Seven sera from patients suffering from typhus, rheumatic fever, malaria, virus pneumonia and tuberculosis were negative, with the exception of one serum from a case of typhus fever which was positive at 1/12.5. All these tests were adequately controlled.

The authors conclude tentatively that fixation of complement in a titre of 1/25 and over should be taken as "diagnostic" of relapsing fever.

The time of development of the specific antibodies and the period of their persistence after apparent cure will be investigated, but in one case it was shown that these antibodies were present in low, though provisionally diagnostic, titre at the end of the first bout of fever. A point of interest is that in four of the six known cases of relapsing fever, blood films were negative for spirochaetes at the time the blood was taken for the complement fixation test.

The authors suggest that this complement fixation test promises to be of value in cases where finding the spirochaete in the blood is unlikely, in surveys of the incidence of relapsing fever, and possibly as a test of cure, though this aspect has not yet been studied.

H J O'D Burke-Gaffney

DEANE, Maria P. Verificação da infecção natural de ratos por *Leptospira icterohaemorrhagiae* na cidade de Belém, Pará [Natural Infection of Rats with *Leptospira icterohaemorrhagiae* in the City of Belém, Pará] *Rev. Serviço Especial de Saúde Pública* Rio de Janeiro 1947, July, v 1, No 2, 261-71. English summary.

In Belém, northern Brazil, the author found a natural infection with *Leptospira icterohaemorrhagiae* in 4 of 15 *Rattus norvegicus*, 4 of 19 *R. rattus* and 3 of 22 *R. alexandrinus*.

Infection was detected by dark-ground examination either of urine or of kidney suspension or both and by animal inoculation. Eight strains were highly virulent for white mice. Of 104 white mice inoculated with infected material, 28 died of causes other than leptospirosis, the remainder were jaundiced and usually showed pulmonary haemorrhages at postmortem. A few mice without jaundice recovered and later showed leptospirae in the urine, two of them were still passing these organisms in the urine after 3 months' observation. Young white mice (3-4 weeks) proved very susceptible as laboratory animals.

Strains from wild rats were grown on Verroot's medium and .5 per cent rabbit serum in the medium instead of 0.5 per cent, provided the best results.

A strain which proved infective to chick embryo appeared to take on increased virulence since after passage, it killed 3 mice in 4 to 5 days, although previously it had killed mice in 10 to 14 days.

No human cases of Weil's disease have been recognized in the Amazon region so far but in view of the comparatively high infection rate in rats in Belém and the potential opportunities for human infection it is important that medical practitioners should have the possibility constantly in mind.

H. J. O'D. Burke-Gaffney

## LEPROSY

INTERM J. LEPROSY. Cleveland, Ohio. 1944 Dec. Suppl. to v. 12, 65 pp. World Wide Distribution and Prevalence of Leprosy

COMTE HAS DUFAR, P. Leprosy in Spain. *Internat. J. Leprosy* Cleveland, Ohio 1947 Apr-June v. 15 No. 2, 18-32.

DE SOUZA ARAUJO H. C. La lèpre en Scandinavie. (*Leprosy in Scandinavia*) *Brev. révis. Méd.* 1947 Dec. 1. 27 No. 51, 2809-10.

DUBOIS A. La lèpre au Congo Belge en 1938. (D'après les rapports et documents de L. VAN HOOB, Médecin en Chef de la Colonie et de nombreux médecins et missionnaires de l'assistance médicale indigène.) (*Leprosy in the Belgian Congo*) *Institut Royal Colonial Belge, Section des Sciences Naturelles et Médicales. Mémoires*. (Collection in-8°) 1940 v. 10 No. 2, 60 pp. 1 map. (Bibliography)

This report gives a shuible summary of the measures for long in use in the Belgian Congo for the control of leprosy, and is based on reports by many medical workers, which should be read by leprologists especially those engaged in similar work in backward tropical areas.

Agricultural colonies for leprosy patients have been instituted in this territory since 1927 mainly under the care of medical missionaries. Since 1937 a Commission has collected information on the endemicity of the disease which was condensed in a report by Dr. VAN HOOB, the chief medical officer on which the present publication is based. The geographical distribution of leprosy is first dealt with: at the end of 1938 the known cases were estimated 1,019 or a mean of about 0.55 per cent of the population. This is considered to be a maximum figure as other skin diseases are sometimes erroneously diagnosed as leprosy. Tables at the end of the report show 18,638 as segregated including many patients with neural disease. It is not possible to say if the incidence is increasing or not. The north shows higher rates than the south. Another table shows 64,534 under treatment. The number of children infected is low except in highly infected areas, and females suffer nearly as much as males. The proportion of lepromatous cases is only 10 to 15 per cent of the whole; the disease is therefore of a mixed type in this region though advanced or tuberculous cases are seen. It is not held that the nerve type is completely non-existent though the main sources of infection are the lepromatous cases.

The report goes on to deal with local variations in incidence and records a detailed survey of three highly infected villages with up to 10 per cent of the occupants infected. The interesting suggestion is made that it would be simpler

in their case to remove the healthy than to isolate all the infected elsewhere. The great difficulties in dealing with a highly infected area of very poor and backward people living in a high degree of general and sexual promiscuity is well brought out. The commonest exposure to infection is domestic. Some differences of opinion are quoted regarding the effectiveness of chaulmoogra preparations and some doctors advocate their intravenous use.

Lastly, prophylactic measures are dealt with and preference is given to agricultural colonies containing about 300 persons frequently visited by a European doctor. At present these colonies contain a large proportion of neural cases, but the question of isolating only the more infective lepromatous patients is under consideration. A Government circular of 1937 on the campaign against leprosy is reprinted in this interesting publication.

L. Rogers

LARA C B. The further Role of the Cullon Leper Colony. *J Philippine Med* 4ss 1947 Oct v 23, No 10 465-71

YBARRA PÉREZ, R & GONZÁLEZ PRENDES, M A. La lepra y el estado civil de los enfermos de lepra en Cuba [The Civil State of Leprosy Patients in Cuba]. *Rev Sifilografía, Leprología y Dermatología* Marianao, Cuba 1947, Apr, v 4, No 2, 72-6

The author gives figures which indicate that the percentage of married persons suffering from leprosy among the sick population in Cuba is 15.67 per cent higher than that of the married persons in the whole of the healthy population of that country, but the percentage of those in hospital is less than that of the ambulatory cases, owing to a number of social conditions.

On the other hand, the percentage of unmarried persons with leprosy among the sick population is 16.58 per cent less than that of the unmarried in the whole population, and the percentage of ambulatory cases is less than that of the unmarried hospital patients.

The social causes and significance of these findings are discussed.

H J O'D Burke-Gaffney

FLOCH, H. On the Epidemiology of Leprosy in French Guiana. *Internat J Leprosy* Cleveland, Ohio 1947, Apr-June, v 15, No 2, 183-8

This is an instructive account of a careful inquiry on modern lines. In the course of 21 years 1,447 cases of leprosy were registered, of whom 1,131 remain, or 51 per cent of the population, a lower figure than earlier estimates. Altogether, 253 occurred among the penal population 157 of whom were Europeans. Early cases have been sought for, and the unregistered cases are estimated not to exceed 300, bringing the total incidence to 6.5 per cent. There were 710 males and 478 females. Children up to 15 years of age formed 43.8 per cent, and persons over 25 years formed only 37.7 per cent of the whole. Examinations of school children showed that 49 per cent of new cases occurred in children up to 15 years of age. Contagion among school children is real and the results of segregating all those discovered resulted in a progressive diminution of new cases in the schools, from 26 in 1939 to only 8 in 1945. The disease is not hereditary and familial infection is a proven fact. A servant had apparently infected five infants under her care. A table indicates transmission to collateral more often than to direct descendants. In children the maculo-anaesthetic form is most frequent, and it is considered to be the least dangerous. On the other hand, Europeans are usually only infected after long residence and with a longer incubation period than in the case of indigenous

children who appear to be more susceptible. The proportion of progressive and serious types is greater in Europeans, who appear to have less resisting power than the indigenous people. This indicates the presence of a relative immunity among the Creole population, who have long been exposed to infection. Mitsuda reactions were positive in 80 per cent. of tuberculoid, 51 per cent. of neural, 1 in 12 of mixed cases, and were negative in all lepromatous cases. In healthy children under 10 years old, no positive reactions were met. An attempt to immunize children by inducing positive reactions is suggested.

L. Rogers

RIZZ, J. B. Frequency of the Clinical Types of Leprosy according to the Natural Regions of Brazil. *Internat. J. Leprosy* Cleveland, Ohio, 1947 July Sept. v 15 No. 3 246-57

Tables are given of the incidence per mille and the percentages of the different types of leprosy in relation to geographical and climatic conditions. The very hot humid Amazon river basin shows the highest rates of 1 to 3.8 per mille but with fewer severe lepromatous cases. On the contrary the dry north-east region has the lowest rates of 0.0 to 0.1 per mille, but with a larger proportion of lepromatous cases. The eastern, southern and west-central regions, with cooler climatic conditions, present intermediate data. The author agrees with Rogers that hot humid climates favour the spread of leprosy and he thinks that they act by adversely affecting the body metabolism rather than by an indirect effect in favouring the transmission of the disease [Rogers suggested that the innumerable insect bites of hot damp climates favour the entry of lepra bacilli from contact cases through the puncture or abrasion lesions of the skin.] The author also suggests that humidity favours a less severe evolution of the disease and that a cold climate favours more acute development.

L. Rogers

MENDONÇA P & MANGRÃO G. Leprosy in the State of Rio Grande do Sul. *Internat. J. Leprosy* Cleveland, Ohio, 1947 July Sept. v 15 No. 3, 254-63.

DUBOIS, A. Classification de la lèpre [Classification of Leprosy] *Ann. Tropica. Basle* 1947 v 4 No. 4 289-97

The author criticizes the classifications of South American workers and that of TISSOT as leaving many difficulties, especially for the clinician, in the neural cases. He suggests classification based on the amount of bacillary invasion of the tissues, as determined by simple routine examinations, rather than on less easily ascertained histological grounds, and suggests the following classification, in which the old symbols are shown after each form in brackets.

A.—Bacilli rare or absent. Subdivisions A M flat macules (Na) A A anaesthetic-acrotic (Na) A M A maculoanaesthetic (Na-Na) A T elevated macules, tuberculoid major (NT) A-t elevated macules tuberculoid minor (Nt) A T A (or t A) elevated macules with lesions of nerves (NT (t)-Na).

B.—Bacilli numerous (++ or + -) B.M. Macular (Lm) B.L. Lepromatous, nodular (L1,2,3) B.I. do. localized infiltration. (L1-3) B.D. do. diffuse infiltration (Ld) B.G. do. generalized B.A. anaesthetic-acrotic (LN) A anaesthetic-acrotic (secondary)

L. Rogers



PORTUGAL, H **Contribution to the Study of the Classification of Leprosy Aspect of Lesions, Antigene Response, and Presence of Micro-Organisms in Histologic Structure** *Internat J Leprosy* Cleveland, Ohio 1947, Apr-June, v 15, No 2, 162-8

In this paper, the practical application of the South American classification is considered in the light of histological examinations in 70 cases, in the majority of which an immediate diagnosis of type was possible. In others, time was required to watch the evolution. Among 13 lepromatous cases, mostly fairly early ones, all were positive bacteriologically and gave negative Mitsuda reactions. Moreover, the lipid staining test was positive except in very early cases. The tuberculoid group included reacting and quiescent cases. One reacting case developed into the lepromatous type during eighteen months; a second remained tuberculoid and in a third the evolution remained doubtful. Among 32 quiescent cases, the majority being of one to six months' duration, all were uniformly tuberculoid and negative bacteriologically to routine examination and all but two were positive to the Mitsuda test. The "uncharacteristic" type numbered 18; they mostly showed achromic or hypochromic spots or merely anaesthetic areas. Only two showed bacteria and half were Mitsuda positive and half negative. In all, only small lymphocytic infiltration was found around the small vessels. In two cases, tuberculoid structure developed later. Re-examinations were not done in a number of these cases, so their evolution is uncertain and no one can foretell their outcome. They may remain "uncharacteristic" or may evolve into tuberculoid or lepromatous cases.

L Rogers

RODRIGUEZ, J N **Observations on the Classification of Leprosy** *Internat J Leprosy* Cleveland, Ohio 1947, July-Sept, v 15, No 3, 274-302 [52 refs]

This is a full discussion of this difficult subject which should be read by all leprologists. The author first traces the evolution of classification from the old Norwegian one of "nodular" and "anaesthetic" up to the recognition of a third or "tuberculoid" type by the Cairo Congress in 1938, based on histology largely due to the work of WADE. This was soon recognized to be still inadequate, especially by South American pathologists, which led to the adoption, by the Second Pan-American Conference at Rio de Janeiro in 1947, of the following types:

Uncharacteristic (I) or Unidentified, Macular, Neural or Neuro-Macular Lepromatous (L), Macular, Infiltrative, Nodular, Neural and Generalized Tuberculoid (T), Macular, Papular, Neural and Reactive

It differs from an earlier South American classification in raising the "uncharacteristic" form to the status of a fundamental type. Its scientific basis is histological, for the uncharacteristic type is characterized by the presence of only simple round-cell infiltration, as opposed to the tuberculoid granuloma and foamy-cell infiltration respectively of the other types.

The present author proposes to add a fourth type, characterized by only interstitial proliferation as found in the maculo-anaesthetic (neuro-leprid) and he calls the second type with round-cell infiltration simple macular (leprid). He further discusses the question of the evolution of tuberculoid into lepromatous disease and accepts the evidence of South American workers who followed the change of typical Mitsuda- or lepromin-positive tuberculoid cases into negative reacting lepromatous cases as proof of such a change although it usually takes a long time to be brought about. He also discusses the difficulty in classifying the common "neural" cases which require further biopsy studies. He suggests that the lepromatous form is the characteristic fully

developed leprosy in non-resisting patients and the other three types are either benign atypical cases or evolutionary forms of the earliest stage of the disease. The histological classification cannot be adopted by the great majority of those working in the field at the control and treatment of the disease for want of time and opportunities for making biopsies. He therefore proposes the following subdivisions of the four fundamental types —

1 *Interstitial*.  $MA_1$  (Mitsuda positive or negative)  $MA_2$  (moderate atrophies, Mitsuda positive) and  $MA_3$  (marked atrophies, paralysis, trophic ulcers, Mitsuda strongly positive)

2 *Perivascular Round-Cell* (Uncharacteristic stage.) Mitsuda plus or minus RCpt pre-tuberculous (lepid) RCpt, pre-lepromatous RCr residual

3 *Tuberculous Stage* (T) (Mitsuda positive) T simple (tuprl or minor) Tm, macular Tmp, maculo-papular or papular Tmn or Tmpa, with nerve involvement TR, reacting tuberculous (major) TRn, with nerve involvement Tr residual Tlar, leprosy leprosy (hyperergic)

4 *Lepromatous* (foamy cell) type (Mitsuda negative)  $C_1$   $C_2$   $C_3$  with or without  $N_1$  or  $N_2$

For further detailed description of the above forms, the original paper must be consulted. A good bibliography is appended. L. Rogers

DR SOUZA LIMA, M. BARBA RUBIO J., DR SOUZA LIMA, L. & RATH DR SOUZA, P. Pathogenic Basis of the South American Classification of Leprosy. *Internat. J. Leprosy* Cleveland, Ohio. 1947 Apr June v 15 No. 2, 169-74

This paper deals with the pathogenesis of leprosy in relation to immunology and the histopathological structure of the lesions, with a view to explaining the mutations from one type to another which occasionally occur. *M. leprae* on entering the human host can survive for long in the interstitial connective tissue without multiplying actively until it succeeds in penetrating into living cells. The bacilli are then phagocytosed by macrophages and histiocytes, which may react by destroying the bacilli by lysis in resistant tuberculous forms or the bacilli actively multiply in the cells to form the typical foamy cells seen in lepromatous cases with little resistance to the invasion. When the body cells remain indifferent and non-reactive the "uncharacteristic" type results for a time. The two types of reaction may occasionally occur in the same lesions as a transitional form of an unstable nature the ultimate development of which is doubtful. In such the action of drugs or other favourable influence may produce a structural change from lepromatous to the tuberculous type. The South American classification is based on clinical, immunological and histological grounds. L. Rogers

ATULAY R. D. The Mitsuda Test in Non-Leprous Persons in a Non-Endemic Country. *Internat. J. Leprosy* Cleveland, Ohio. 1947 July Sept. v 15 No. 3, 264-8.

1 Among 73 American adults of both sexes but predominantly Negroes, 74 per cent reacted positively to full strength lepromin, but only 33 per cent to a 1:10 dilution of the same lepromin.

2 Among males, 63 per cent reacted positively and among females 83 per cent.

3 Concentration of bacilli in the antigen is important and should be standardized if results are to be compared.

4 The authors believe that the mechanism of the Mitsuda phenomenon is due to a basic constitutional activity of the tissues. This natural tissue response may be accelerated either by *M. leprae* or *M. tuberculosis*.

PORRITT, R J & OLSEN, R E Two Simultaneous Cases of Leprosy developing in Tattoos *Amer J Path* 1947, Sept, v 23, No 5, 805-17, 8 figs on 3 pls [10 refs.]

This is an important contribution to the disputed question as to the inoculability of leprosy. The authors quote the opinion of JEANSELME that there is no adequate proof of the transmission of leprosy by inoculation, and also cites cases reported by ROGERS and MUIR to the contrary effect. They now record the cases of two men of the U S A Marine Corps, who were tattooed successively by the same man on the same day in June 1943, at a time when both the soldiers and the tattooer were drunk. Two and a half years later, in 1946, both men developed discoloured anaesthetic patches around the new tattoo marks, but an earlier tattoo mark in one was not involved. Portions of the lesions were removed for examination in both men without any discomfort in spite of the fact that no anaesthetic was used. Guinea-pigs were inoculated, with negative results as regards tuberculosis. Sections of the tissues of both showed typical tuberculoid changes, scattered acid-fast bacilli were readily found in one and less frequently in the other. The second patient developed similar patches on his other arm subsequently to those at the site of the tattoo mark. Sections of both were sent to the Carville Leprosarium, the authorities of which came to an unequivocal diagnosis of "typical tuberculoid leprosy". Both the naked-eye and the microscopical characters of the lesions are illustrated by plates.

The authors conclude that "These two cases provide strong evidence for the spread of leprosy by inoculation"

L Rogers

SCHUJMAN, S Therapeutic Value of Chaulmoogra in the Treatment of Leprosy *Internat J Leprosy* Cleveland, Ohio 1947, Apr-June, v 15, No 2, 135-45, 6 figs on 2 pls

The author stresses the necessity of early treatment of lepromatous patients by large doses of chaulmoogra oil regularly continued until the patients have remained free from symptoms for some time. He writes from seventeen years' experience and deals only with lepromatous cases, because other forms may recover spontaneously. He thinks reported failures are due to deficient doses and duration of the treatment. He finds that untreated lepromatous cases always become worse and those treated irregularly show an unfavourable evolution, but previously untreated cases nearly always improve, often rapidly, although renewed treatment after an interval is less certain and slower. Cases not benefited by small doses are benefited by larger ones and may become bacteriologically negative. The proper method is to inject the maximum amount which can be tolerated in the minimum time. All hospital patients who became clinically and bacteriologically negative had received a total dosage of 1,500 cc of ethyl esters, preferably with 4 per cent creosote, but of those showing only slight improvement, only 27 per cent had received the full dosage. The injections are made intramuscularly and intradermally. With the full dosage, 40 per cent of all treated lepromatous cases have been rendered clinically and bacteriologically negative, and 40 per cent have become definitely, and not only slightly, improved with the injection of a total amount of 30 cc weekly. The author is of the opinion that over 80 per cent of failures in lepromatous cases are due to deficient dosage and irregular treatment. The few failures are nearly all very advanced cases. Illustrative photographs of patients before and after treatment confirm the author's claims.

L Rogers

DE SOUZA-ARAÚJO, H C Le Promin dans le traitement de la lèpre [Promin in the Treatment of Leprosy] *Liber Jubilaris J Rodham (Soc Belge Méd Trop Brussels)* 1947 Dec 195-200

FLOCH H. & CAMA W. R. Sur le traitement de la lèpre par la Promina, en Guyane Française (The Treatment of Leprosy with Promina in French Guiana.) *Institut Pasteur de la Guyane et des Territoires de l'É. M.* Publication No. 169 1947 A g 8 pp

ROSS, Hilary Blood and Urine Concentration of Promina Disease, and Promina in the Treatment of Leprosy. *Internat. J. Leprosy* Cleveland, Ohio. 1947 July Sept. v 15 No. 3, 236-45 2 figs.

WHARTON L. H. Preliminary Report on a New Sulphonamide Drug "Sulphetrons" *Internat. J. Leprosy* Cleveland, Ohio. 1947 July Sept., v 15, No. 3 231 S.

Sulphetrons in 3.0 Gm. daily dose giving 1 tablet (0.5 Gm.) every four hours has proved to be safe. We have seen only very mild toxic effects from the drug nausea, which was quickly relieved by administering sodium bicarbonate, 30 gr three times a day orally. There has been marked improvement in clinical symptoms, with flattening out of nodules. Bacteriological smears from nose and skin have shown marked improvement from month to month and one patient with positive nose and skin smears became bacteriologically negative in the fifth month.

It should be noted that this trial was made on early  $L_1$  cases that were free from any complications of the disease. Clinical trials continue and will be extended to include patients with more advanced lesions, and with complications.

FAGET G. H. & ERICKSON P. T. Use of Streptomycin in the Treatment of Leprosy. A Preliminary Report. *Internat. J. Leprosy* Cleveland, Ohio. 1947 Apr-June, v 15 No. 2, 148-53.

The antibacterial action of streptomycin against the tubercle bacillus led to this trial. In 1945 the receipt of 50 million units allowed of only one patient being treated the results were encouraging but not definite after several months. In June 1946 sufficient streptomycin to treat 10 cases was received and  $\frac{1}{2}$  gm. or 250,000 S. units were injected every three hours for four months in 8 of the patients. Unpleasant and even serious toxic effects were observed, the most frequent being vertigo with lasting deafness in one, eosinophilia, anaemia, loss of weight and low blood pressure fever headache and casts and blood cells in the urine due to renal irritations. The drug requires further purification. Improvement was noted but was not greater than that achieved with less toxic sulphonamides. It is too soon to judge of the value of streptomycin treatment. L. R. 108

FITE G. L. ERICKSON P. T. GEMAN F. & JOHANSEN F. A. Local Treatment of Leprous Ulcers with Crude Preparations of Streptomycin. *Internat. J. Leprosy* Cleveland, Ohio. 1947 Apr-June 15 No. 2, 154-61 11 at fig & 1 fig on 3 pls

Crude filtrates of *Streptomyces griseus* of local manufacture have been tested on leprosy ulcers with promising results. The original paper should be consulted by those interested in the method of culture. The filtrate contained 28 to 40 microgrammes of streptomycin per cc. and was used by soaking layers of gauze with it and applying them to the ulcers with a protecting layer of rubber to prevent excessive drying. The gauze is soaked every twelve hours for a week and then renewed weekly until the ulcer is healed, provided that no irritation is produced. If erythema with vesiculation is produced, the filtrate

should be diluted 1 in 5 with boric acid. Thirty-six patients have been treated and in only one did toxic symptoms necessitate stopping the applications, and another patient objected to the bandaging. Notes of illustrative cases are given. They are divided into three groups. In group I, consisting of perforating ulcers of the sole of the foot, success was obtained in 18 out of 19, in mixed cases, in 11 of 14, and in the only lepromatous case treated. Sloughing varieties show most resistance to the treatment and complete healing was only obtained within two months in 45 per cent. Trophic ulcers respond best. Of the total cases, one-fourth healed in less than one month and 70 per cent in two months. The results are therefore satisfactory. Photographs of cases before and after treatment are recorded.

L. Rogers

## HELMINTHIASIS

FEROLA R. Sulla frequenza della parassitosi intestinale nell'infanzia. [The Incidence of Intestinal Parasites in Children] *Pediatrics* 1946 July-Sept, v 54 Nos 7/9, 426-31 [11 refs] English summary (6 lines)

A survey of 244 children in Naples

BASSÈRES M S & PANTOJA W P. Vermunoses—Algumas considerações em torno das verminoses na área do Rio Dóce. [Observations on Worm Infestations in the Rio Dóce Area, Brazil] *Rev Serviço Especial de Saúde Pública* Rio de Janeiro 1947 July v 1 No 2 235-49 1 map & 4 figs. English summary

CAUSEY O R, COSTA O & CAUSEY, C E. Incidência de parasitos intestinais do homem em Belém, Pará e vizinhanças. [Incidence of Intestinal Parasites in Man in Belem, Para and its Environs] *Rev Serviço Especial de Saúde Pública* Rio de Janeiro 1947 July v 1 No 2 221-33 5 figs. English summary

DA COSTA O R. Incidência de parasitos intestinais em quatro cidades da Amazônia. [Incidence of Intestinal Parasites in Four Cities of Amazonia] *Rev Serviço Especial de Saúde Pública* Rio de Janeiro 1947 July v 1 No 2 203-19 5 figs. English summary

WILKINS, A J W. Schistosomiasis in Salisbury, S Rhodesia. *Pub Health* Johannesburg 1947, Nov v 11, No 11, 4-6 9-10

This paper was read to a Health Officials' Congress in Southern Rhodesia by the M O H of the capital city, Salisbury.

He gives figures from the health department files concerning African patients, showing that on single microscopic examinations 30 per cent of 13,000 urines and 8 per cent of 9,400 stools were positive for bilharzia eggs. He believes [probably rightly] that the true infection rate is much higher than this and goes on to discuss measures for its amelioration. Like most workers with primitive peoples he despairs of an immediate public response to the provision of sanitary facilities, although he notes that in Salisbury, where numerous conveniences have been provided there has been a considerable reduction in promiscuous fouling. He also feels that the numbers requiring treatment are too great for his department to be able to rely on mass treatment of infected people as a control measure. He has therefore set out to kill the bilharzial snails [he names

*Physopsis globosa* but it is not certain whether this species or *P. africana* is more important) in the water around Salisbury and he reports success with a copper-sulphate-bag method, as follows —

"The salt of which the larger lumps have been broken, is placed in a small bag of cloth mosquito netting, cheese cloth or organdie which is attached by string or wire to a stick. The bag is then dipped in and out of the water along the sides of the pool or stream particular attention being given to water in the vicinity of reeds or other grasses. In our experience it has been found that by moving along the bank fast enough to allow the bag to be submerged in the water and withdrawn immediately, and for this to be repeated at approximately 1" to 18-inch intervals when the flow is not too rapid or very considerable in volume the concentration obtained has proved sufficient to kill 100% of the snails present.

[It must however be pointed out that this bag method is not a universal application. While no doubt satisfactory where river-banks are fairly level and well-defined or in ditches or irrigation canals, it is of little value in the treatment of "wild" river-courses, with their broken and irregular banks. The author himself points out that the bag method is being used in favourable conditions.]

He makes the interesting observation that it has been found possible to use his "anti-malarial gangs" on this snail destruction work a great saving in expenditure.

His work shows that it is apparently possible to protect a small area in an infected country when this is desirable because of the large concentration of people living in that area.

(14 Apr)

ZITO P. Tentativi di infestazione di molluschi nutriti con uova di *Schistosoma haematobium*. Osservazioni sulle uova ed azione di alcune sostanze su esse e sul miracidio. (Observations on the Infestation of certain Molluscs with *S. haematobium* — the Effects of Different Substances on the Eggs and Miracidia. *Atti Med. Italiana*, 1947 Dec. — No. 12, 375-7)

The English summary appended to the paper is as follows —

"The author describes the characters of the molluscs intermediate hosts of some trematodes which infest man — he reports on some negative attempts of infestation of molluscs (*Planorbis cornutus* Phil. ? *Physa* fontinalis *Hebertia corniculata*) with eggs of *Schistosoma haematobium* — he exposes some observations on the eggs of *Schistosoma haematobium* and its miracidium and on the action of some substances (cosm. trypanflavine, penicillin) on them — cosm. trypanflavine kill the embryo — penicillin has no effect on the time of opening of the eggs and on the miracidium.

COMBER, S. G. Observations on the Life-Cycle of *Schistosoma mansoni* in the Laboratory with a Discussion on the Snail Vectors of *S. mansoni* and *S. haematobium*. *J. Trop. Med. & Parasit.* 1947 Sept. v. 41 No. 2, 173-7. [14 refs.]

The author writing from the Liverpool School of Tropical Medicine, has succeeded in establishing strain 1 *Schistosoma mansoni* in a monkey after having infected strain of *Planorbis* boursin with miracidia obtained from infected larvae of patients who acquired the disease in Uganda. These snails were from an Egyptian stock and the author also succeeded in infecting *Amnatia galathea* the tropical American intermediate host. He describes the technique adopted, which was perfectly simple.



*Bul nas forskali* (Ehrenberg) but has not found any living specimens. He also mentions a number of other snails which are not, so far as is known, concerned in human schistosomiasis.

Charles W. Brooks

GIAGIS B. & ARIZ, S. Treatment of Schistosomiasis. *Lancet*. 1948, Feb. 7 208-9 1 fig.

The authors have investigated the action of sodium antimony tartrate in the treatment of schistosomiasis, following the method of Alves and Blair with minor modifications.

The total dosage of (freshly prepared) sodium antimony tartrate was 1 gram for every 5 kgm. of body weight and was divided into six more or less equal doses, which were given on two successive days at 8 a.m., 11 a.m. and 2 p.m. Special precautions were taken to give the injection slowly. The drug was prepared in a solution of 1 grain in 1 cc., and out of 18 patients, 12 received the dose undiluted, but in 4 it was made up to 10 ml. with 5 per cent. glucose solution. All-glass "Record" and "Lum" syringes were employed.

The immediate reactions are described as rather severe and in some cases drastic, whether the drug was diluted or not. The commonest were cough, vomiting, tightness of the chest, pyrexia and pain in the arm or shoulder, sometimes pain in the joints, toothache, a metallic taste in the mouth, a sense of irritation in the bladder or peculiar chondriform movements of the arms and legs. On the whole, the patients had no appetite and preferred to stay without food for the two days of treatment. They invariably looked ill and dreaded the injections. Out of 18 cases, 6 had a mild bradycardia after each injection. A minor drop in the systolic blood pressure was sometimes registered. Electrocardiographic records were made of every patient before treatment, at the end of the first and second day's treatment, and again within the following week. Changes in the QRS complex and T wave appeared at the end of the first day, becoming more pronounced as treatment proceeded. These changes were restored about the second day after treatment.

The haemoglobin percentage tended to rise during treatment and this was ascribed to haemoconcentration. All patients showed a loss of 1-3 kgm. in weight during the same period, but regained it within 10-14 days. In *S. haematobium* infections, the patients continued to show haematuria until the 10th day after treatment but by the end of the second week all testified to the relief of urinary symptoms. On the second day after the end of treatment all patients were still passing living ova. By the 23rd day any ova passed were dead, but in five instances they were passed continuously for eighty days. Observations on these ova appeared to indicate that although temporarily damaged by antimony some worms survive and, after a period of cessation of oviposition, recommence reproduction. Dead ova are best demonstrated by sedimentation methods. In this state they are wrinkled, distorted and smaller than normal.

The difficulties of application of the two-day treatment in large-scale campaigns are obvious, therefore 9 patients were treated with the same doses spread over a six-day period.

On the whole the reactions were fewer and milder. The urine was examined after the third injection, five days after the end of treatment and subsequently at weekly intervals. Three patients were passing ova on the 16th day and by the 33rd day living ova were detected in two.

The relapse rates in these two methods was 31 and 33 per cent. respectively. While admitting that the two-day treatment of Alves is an advance over the original method, the authors consider it to be too drastic to be useful in large-scale campaigns.

P. M. Mason-Baker



NESS, A T, BRADY, F J, COWIE, D B & LAWTON, A H Anomalous Distribution of Antimony in White Rats following the Administration of Tartar Emetic. *J Pharm & Exper Therap* 1947, June, v 90, No 2, 174-80, 1 fig

"Dogs and rats were injected with tartar emetic prepared from radioactive antimony. Antimony concentrations in the blood and tissues of rats were considerably different from those in dogs and, judged by available data, were also different from concentrations encountered in man, white mice, cotton rats, and hamsters.

"In white rats, the blood antimony is characterized by an increasing concentration beginning at 8 hours and lasting at least for 72 hours. This is in contrast to that in man and in the dog in which the concentration is decreasing to very low levels at these intervals.

"There is some indication that the antimony compound appearing in the blood of the white rat at later intervals is considerably less toxic to the rat than its tartar emetic precursor. It is suggested that results obtained in screening antimonial compounds in white rats be interpreted with caution until more is learned of the phenomenon."

LUTTERMOSER, G W The Control of the Blood-Fluke Disease (Schistosomiasis) in Venezuela. *Health & Sanitation Division Int Inter-American Affairs Newsletter* Wash 1947, Oct (Schistosomiasis Number) 24 pp, 25 figs & 3 maps

This Newsletter is, no doubt, written largely for the non-medical reader, but its author is already well known for his work on the subject, and his description, based on his own experience, is comprehensive and most informative. The publication is a succinct account of control measures, and could hardly be bettered. Luttermoser himself has returned to the United States (he is a graduate of Johns Hopkins), but no doubt his methods will be continuously developed in Venezuela.

The area of schistosomiasis in Venezuela lies within a semicircle of 100 miles' radius, whose centre is at Catia La Mar, there are coastal foci and foci along the main drainage systems, and they involve a population of over one million. It has been estimated that there are more than 50,000 cases of schistosomiasis (*S. mansoni*) in the country. Diagnosis is made by faecal examination by skin test with extract of adult *S. mansoni*, and at post mortem examination. (JAFEE at the Hospital Vargas had found it to be the cause of death in 54 per cent of 2,461 autopsies, that it was present in 18 per cent, and that of those with the disease, 37 per cent died of it.) Treatment is given to infected persons at the various clinics, and tartar emetic and Fouadin are used.

Eradication of *Australorbis glabratus* (the snail host) includes the clearance of vegetation from irrigation canals, and the training or paving of the bed and banks of these canals, to increase the rate of flow. Water holes are filled in or drained and copper sulphate or carbonate, or freshly-slaked lime, are applied where necessary. In some sections irrigation ditches are placed in conduits where they run near houses, so as to protect them from fouling. Latrines are constructed and the people are educated in their use and instructed in the mode of infection. The disease is most prevalent among the poorer people, and it is thought that general education may be a potent force in reduction of infection.

An account is given of the various surveys made at Maracay, the El Valle river system and the Guarenas region. Snails occur in rivers where the current is slow and where there is much vegetation, optimum temperature is about 20°-26°C. Flooding may wash snails downstream into water holes or irrigation

canals. It was found (as had previously been known) that a standard sand filter will not hold back cercariae, but that standard chlorination of water if carefully controlled, will destroy them.

Snails are found in great numbers in watercress gardens, sugar-cane plantations and other similar cultivated areas. Watercress cultivation is a most important industry—the method adopted to eliminate the snails was to remove all vegetation from the beds (each about 1/2 square yards) and treat them with freshly slaked lime and dry them thoroughly in sunlight. The banks were built up and the irrigation inlets and outlets were strengthened. The snail eradication work was begun at the head waters and continued downstream, and the watercress gardens were mostly in the upper reaches. New plants were carefully washed in lime water before planting.

A reed is grown in these upper reaches, which is used for animal packs—snail control in these gardens consisted largely of drying every 3 months and applications of copper sulphate. Workmen are advised to wear rubber boots, and efficient latrines are provided.

The author thinks that control is possible by more extensive and intensive use of the measures discussed, but he places special emphasis on health education and sanitary improvement.

Charles W. Stocks

REEVES D. L. & HERR, R. W. *Schistosomiasis Japonica with Intracerebral Granuloma: Operative Removal with Recovery*. Report of a Case. Arch. Neurol. & Psychiatry 1947 Aug., v 68, No. 2 207-20 3 figs. [12 refs.]

In the literature on *Schistosoma japonicum* there are reports in only two cases of the successful surgical removal of intracranial granulomata attributable to this parasite. Both the patients made good clinical recoveries. A patient of the authors a soldier of 29 when serving in the south west Pacific area, developed diplopia, headache and recurring convulsive seizures with loss of consciousness, in January 1945. In August 1945 a detailed physical examination revealed little more than bilateral papilloedema slightly impaired stereognosis on the left side and some weakness of the left hand grip. The cerebro-spinal fluid was at a pressure of 430 mm., but was otherwise normal. Subsequently ventriculographic study showed displacement of the ventricular system to the left with similar displacement of the third ventricle. There was a noticeable filling defect in the posterior and temporal parts of the right lateral ventricle which was flattened and depressed. A diagnosis of an intracranial expanding lesion in the right temporo-occipital area was reached, and as the patient had a history of a minor head injury in December 1944 the origin was considered to be a subdural haematoma.

Craniotomy was performed in the right occipito-parietal region. The dura was tense, and, on opening it small whitish tubercles from a pin-point to a pin-head in size were seen on the surface of a tumour which was indurated and rubbery. This was removed piecemeal and was found to contain small calcified areas. The tumour was about the size of an orange and extended into the subtemporal area. It was thought to be an unusual type of glioma.

On pathological examination, many *S. japonicum* eggs were found in a granulomatous mass with large areas of caseous necrosis. There were scattered giant cells, and varying degrees of infiltration with eosinophils and with mononuclear phagocytic cells. Over the surface of the tumour there was thickening of the leptomeninges, with increased vascularity and some leucocytic infiltration.

On further questioning, in view of the pathological diagnosis it was found that the patient had probably acquired his infection in Levant in October or November 1944. Examination of the stools failed to reveal the presence of ova. He was treated with courses of stilbophen and of antimony potassium tartrate.

and with potassium iodide by the mouth. The patient's recovery after the operation was uneventful, and in June 1946 he complained only of some general weakness and occasional headaches particularly on the right side and at the back of the head.

The authors conclude with a brief historical review of the discovery of Asiatic schistosomiasis, and a consideration of its causation, symptomatology and treatment. They point out that their case presented none of the expected symptoms and signs of the disease, and so the correct diagnosis was not suspected until revealed by the pathologist. The importance of the condition is apparent in view of the large numbers of United States troops who served in the south-west Pacific and other endemic areas.

A R D Adams

VARTIAINEN, I & BASTMAN-HEISKANEN, L. On the Staining of *Diphyllobothrium* Ova. *Ann Med Intern Fenniae* 1947, v 36, No 3, 729-39 [11 refs]

"The ova of *Diphyllobothrium latum* behave differently in eosin solution. Some are stained red, while others remain colourless. This is true both of ova found in the excrements of worm carriers and of eggs taken from the tapeworm itself.

"The percentage of stained eggs is lowest in the first metres of the worm, but grows higher toward the end part of the parasite, and may then be as high as one hundred per cent. Correspondingly, the number of living larvae is highest in the first metres and very low in the last. The ability of staining undoubtedly means that the ovum is dead, and this may be regarded as indicating decreased vigour in that part of the parasite.

"In all, seventeen worms were examined in order to find out how far the ova were stainable in the different parts of the worm. In this respect, there were differences between the individual worms."

TOTTERMAN, G. Is the Broad Tape-Worm the Causal Agent of Hypochromic Anemia? *Ann Med Intern Fenniae* 1947, v 36, No 1, 185-90 [13 refs]

It is established, says the author, that *Diphyllobothrium latum* may cause typical pernicious anaemia in some of its carriers. In a far greater number, however, there is a "hyperchromic, or an almost normochromic mild anaemia" and these latter cases are cured by a vermifuge and should therefore be considered as being due to the tapeworm. Opinions vary about the relation between hypochromic anaemia and this tapeworm. The history of these questions is briefly discussed with references to the literature.

The author himself studied 43 cases, 34 females and 9 males, with hypochromic anaemia and *D. latum*, most of them had other diseases as well. Thus, 23 had acute infections which included pneumonia, exudative pleurisy, pyelitis, acute polyarthritis and acute nephritis. Three patients had chronic infections and 2 had tumours. It is, the author says, "highly probable" that in these cases the complicating diseases and not the worm caused the hypochromic anaemia. But 10 patients had no complicating diseases. Nine of these had "anaemia achylia simplex" and one had chlorosis.

The author discusses these, his general conclusion is that no single case of hypochromic anaemia in his series was definitely improved by a vermifuge.

alone that the presence of *D. latum* does not seem to impede the spontaneous improvement of the blood picture after an infection or to check the effect of iron in a post-haemorrhagic or an essential hypochromic anaemia and that broad tapeworm anaemia and hypochromic anaemia are not causally connected. This is probably the reason why the combination of broad tapeworm and hypochromic anaemia is relatively infrequent especially in comparison with the frequency of hyperchromic anaemia and broad tapeworm. [See also this *Bulletin* 1948 v 45 97 188, 260]

G. Lapege

HIRVONEN M. Observations throwing Light on the Pathogenesis of Paralcidosis Tapeworm Anaemia. (*Ann Med Intern. Fenn. sc.* 1947 v 36, No. 1 53-65 4 figs. [11 refs.]

*Dephylobothrium latum* is the author says very common in Finland, yet people infested with it seldom have anaemia. EHRESTRÖM, quoted by von Bonsdorff cited below calculated that only 1 patient in 5 000 to 10 000 is ill with tapeworm anaemia but SEPPÄ's (*Duodenosc.* 1927 v 43, 101) estimate is 1 in 459 and TÖRTTÉN's 1 in 113 to 1 in 383. SALTZMAN (*Acta Med. Scand. nava* 1924 Suppl. 7 p. 268) and von BONSDORFF (this *Bulletin*, 1940 v 37 215 216 and 1944 v 41 583 594 and *Scand. Med.* 1941 v 1, 2877) ascribe this incidence either to an abnormal character of the worm or to a constitutional disposition of the host. The latter explanation was supported by SCHRAUMAN (quoted by von Bonsdorff and Saltzman) but has not been proved. The present author describes one case which in his opinion, "indicates very clearly that the abnormal character of the worm decidedly influences the genesis of tapeworm anaemia. This case was a woman aged 23 whose anaemia disappeared after administration of filicin, which failed to remove the whole worm—she had no anaemia when she returned 1½ years later for further treatment for removal of what the author considered to be the same tapeworm. He suggests that the anaemia in this case may have been caused by some disease of the tapeworm and that the anthelmintic may have cured this, so that the patient's anaemia disappeared.

Three other patients are also discussed all of whom had free HCl, so that pernicious anaemia was absent. In all three cases blood regeneration ceased after the worm cure and only continued when liver treatment was given. Examination of these cases 4 8 and 7½ months respectively after cessation of the liver treatment showed that all were completely healthy. The author discusses these cases in relation to the view that *D. latum* destroys all the anti-anaemic liver factor at the patient's disposal and suggests the alternative hypothesis that the worm poison has a paralyzing effect upon the blood forming organs, the bone-marrow and the liver which were strong enough in these 3 cases to begin regeneration of the blood but not strong enough to complete this without the help of liver treatment.

G. Lapege

BACHMANN A. Situation de l'ankylostomose au centre minier de Khouribga en 1945. [The Ankylostome Problem in the Khouribga Mines in 1945.] *Bull. Inst. Hyg. Maroc* 1945 v 5 75-83

In the phosphate mines at Khouribga in 1908 in two sections parts I a mine 68.68 per cent and 40.51 per cent of the workers respectively had ankylostome infection—it was heavy in 8.9 and 1.2 per cent, medium in 33.37 and 13.66 and light in 26.68 and 25.65 per cent. The number of healthy workers infected within 6 months was 65.63 and 20.17 per cent respectively.

As a result of prophylactic procedures by the end of 1941, there were no heavily infected workers, only 21.7 and 16.1 per cent of lightly infected carriers and the chances of contamination in 6 months were reduced to 9.9 and 3.6 per cent respectively.

The remaining 109 lightly infected carriers in the two *recettes* had only an average of 10 eggs per ml of stool and were healthy. During the next four years, their number was reduced to 70, 30, 13, and 6 successively while the numbers of the workers had risen from 885 to 3,132. By 1945 no parasite-free workers became infected after working 6 months in the mines.

This improvement was achieved by two procedures: (i) the treatment of all the medium and heavy carriers, and (ii) the construction of double trench latrines, 1.50 metres wide by 3 metres deep, at various points in the mines so that no worker had to go more than 400 metres to use one.

The latrines and the surrounding earth were periodically disinfected with cresyl and chloride of lime, and the latrines were abandoned long before the contained faecal matter reached the level of the galleries.

For sterilizing the carriers, the author found *Essence de Niaouli* and oil of chenopodium quite useless, and male fern, thymol and carbon tetrachloride very inadequate. Tetrachlorethylene was reliable, he gave it in 1-gramme capsules for three days, 3 grammes on the first day, 4 grammes on the second and 5 grammes on the third, followed three hours after the last dose by 40 grammes of sulphate of soda. By this means he obtained expulsion of worms in 100 per cent, complete removal of infection in 87, and partial removal in 13 per cent of those treated.

The author used the book on ancylostomiasis by GARIN, ROUSSET and GAUTHIER for constant reference, and adapted their teaching to the local conditions.

L. E. Napier

PANTOJA, W. P. & BASSÈRES, M. S. Verminoses — Tratamento em massa pelo hexyl-resorcinol [Mass Treatment of Worm Infections by Hexyl-Resorcinol] *Rev. Serviço Especial de Saúde Pública* Rio de Janeiro 1947, July, v. 1, No. 2, 251-60.

The English summary appended to the paper is as follows —

"1 A total of 7,341 people, including all age groups from 2 years up were treated in mass treatment campaigns in labor camps and small villages in the states of Espírito Santo and Minas Gerais, during 1944 and 1945, using the hexyl-resorcinol 'crystoids'.

"2 In a group of 117 children, apparently healthy, living in a leprosarium preventorium, in which the mean egg count (Stoll-Hausheer) showed 2,630 hookworm eggs per cc, two treatments by the standard dosages showed a reduction of 85.2 per cent from the mean number of eggs found in the first examination. It is emphasized that in spite of the relatively low reduction of hookworm eggs, after two treatments, the hexyl-resorcinol should be the drug employed in rural areas where there is a high prevalence of associate hookworm and ascariis infections. The mass treatment campaign is the method of choice and should be built around the drug, to take full advantage of its atoxicity and remediate [sic—? compensate for] its apparently low reduction of hookworm following a single treatment.

"3 Except for extremely rare manifestations of slight abdominal discomfort, and some allergic reactions, probably due to dead ascariis, no untoward symptoms were observed."

- i. DAVIDSON A. G. BARON BENNE & WALKER, M. Factors influencing Reagin Formation in Experimental Human Sensitization to *Ascaris lumbricoides* Antigen. I. Influence of Chronic Infection (Tuberculosis) on Rate of Sensitization. *J Allergy* 1947 N. v. 18, No. 6, 359-64, 3 figs.
- ii. KALLIN Ekose W. DAVIDSON A. G. & WALKER M. II. The Influence of Sex as a Factor in Rate of Sensitization. *Ibid.* 369-72, 1 fig.
- iii. — — — & — — — III. The Influence of Race as a Factor in Rate of Sensitization with further Observations on the Sex Factor. *Ibid.* 373-80, 3 figs.

This is a study on allergy and the relation to *Ascaris* infection is not considered.

i. FULLEBORN and HILGUTH [this *Bulletin* 1930 v. 27 956] and others have shown that sensitization of the skin to *Ascaris lumbricoles* could be induced in man. The antibodies responsible for the immediate skin reactions in *Ascaris* hypersensitiveness are atopic reagins.

In these studies the extract was prepared from *Ascaris lumbricoles* (pg). The worms were first washed in water afterwards in toluol. "They were then covered with a slight excess of buffered saline and with a layer of toluol. This was allowed to stand at room temperature until most of the worms had disintegrated. The material was paper-filtered and sterilized by Seitz filtration on June 2, 1933. The extract was bottled, covered with a layer of toluol, and stored in the ice box. On September 3 1933 it was again passed through a Seitz filter. At this time the total nitrogen content determined by the macro-kjeldahl method was 5.3 mg. N per ml. From this stock material, proper dilutions for use in this study were made."

The experimental subjects were selected by giving a test dose of 0.025 ml. of an extract containing 0.1 mgm. of N per ml. Only persons giving a negative reaction were used. Sensitizing doses of 0.1 ml. were given at intervals of one week until complete sensitization was effected, or 12 doses had been given. A positive reaction was indicated by the formation of a wheal and erythema.

About one third of the persons given the test dose showed positive or doubtful reactions and were excluded from the experiment.

The sensitization developed in the rest at a variable rate: 19 per cent became sensitive at the time of the third sensitizing dose ( $S_3$ ), 54 per cent. at  $S_4$ , 81 per cent at  $S_5$ , and 92 per cent. at  $S_{12}$ .

Chronic tuberculous infection was not a factor influencing the rate of development of sensitivity but sensitivity developed more rapidly in males than in females. The number of positive reactions was higher by about 2.5 per cent. in males than in females between the  $S_5$  and  $S_8$  but the final percentages, i.e. at  $S_{12}$ , were equal in the two sexes.

ii. The observation made in the earlier investigation that earlier sensitization to *Ascaris* antigen develops earlier in the male was confirmed, and it was incidentally indicated that there is earlier sensitization to the antigen in the Negro race than in white persons.

iii. Further confirmation was obtained of the earlier sensitization to *Ascaris* antigen in negroes compared with white persons and males compared with females. There was no correlation between the rate of sensitization and the natural sensitivity in the four population groups which was undoubtedly but not demonstrably associated with present or past helminthic infection. There was no correlation between rate of sensitization and age. L. E. Vajner

FRANKS, M B, CHENOWETH, B M, Jr & STOLL, N R Reactions of Natives of Okinawa and of American Personnel, to Skin Tests with Test Antigen prepared from Microfilariae of *Dirofilaria immitis* *Amer J Trop Med* 1947, Sept, v 27, No 5, 617-32, 3 figs & 2 graphs [18 refs]

After a brief review of the relevant literature, the authors describe skin tests done from July to October, 1945, on the island of Okinawa. Antigens were made from the adults (females only) and microfilarial larvae of *Dirofilaria immitis* of the dog and from *Ascaris lumbricoides* obtained at necropsies in a Guam hospital. For the methods of making these antigens, the paper must be consulted. *Trichinella spiralis* antigen was supplied by the National Institute of Health. This and saline containing 1/10,000 merthiolate (used to preserve the other antigens) were used as controls. References are given to the methods of counting the helminth eggs in faeces, and the number of microfilariae.

Skin tests were done on more than 400 patients in two natural groups. Group I were service personnel. Sixty of them, stationed on Guam, had not previously been outside the U S A and were not known to have been in areas in which filariasis is endemic; fifty-three had no intestinal helminths, 7 were lightly infected with these. Group I included also 9 patients with a clinical diagnosis of filariasis. Group II consisted of natives of the endemic area of Okinawa considered to be fairly representative of the island's population.

Details are given of the method of doing the skin tests and other examinations of the patients. Examination of a random sample of 677 Okinawans showed that 26.6 per cent had circulating microfilariae and that 57 per cent of 259 Okinawans with this degree of microfilaraemia had physical signs attributable to filariasis. A table illustrates the increased incidence of physical signs with increasing ages, a fact which was considered in the interpretation of the skin tests. Diagnosis was conservatively made on involvement of lymph nodes and channels, the extremities and the scrotum and may have placed the incidence of physical signs too low. Only 8 persons examined (rather more than 1 per cent) had elephantiasis, which was no functional handicap to 4 of the 8. As only 20 other cases of elephantiasis were seen and only one of these was multiple, the usual assumption that filarial infestation and elephantiasis go hand in hand was not confirmed in Okinawa. Combined blood and chemical studies indicated a demonstrable incidence of filariasis in Okinawa of 65 per cent and probably this is considerably higher. The authors concluded, in fact, that they were justified in considering all Okinawans, except very young infants, to be infected.

No intact adult worms were found, but the nocturnal periodicity of the microfilariae and examination of stained smears of them showed that the infecting species was *W bancrofti*. Microfilarial counts of blood drawn between 8 and 10 p m from 180 patients varied from 1 to 23,000 microfilariae per ml; 80 per cent of cases had 1,000 or less per ml and only 6 per cent had 4,000 or more per ml. Positive examinations for microfilariae increased significantly with age, especially when children of 6 to 15 years (19 per cent) were contrasted with adults aged 46-74 years (34 per cent), the corresponding figures for incidence of physical signs in patients with microfilaraemia being 38 per cent and 95 per cent and in patients without microfilaraemia 40 per cent and 73 per cent. There was no positive correlation between the numbers of circulating microfilariae and either the age of the patients or the degree of clinical filariasis. Of the 8 patients with elephantiasis, 4 had circulating microfilariae but in 3 of these the elephantiasis was minimal (*cf* above).

For details of the results of the skin tests the paper itself must be consulted. An important net result was the confirmation of the conclusion of earlier workers that an antigen made from microfilariae of *D immitis* has a limited use as a diagnostic aid in filariasis. It is more specific in the sense that fewer false





mode of action of filaricides the trial and error method of approach seemed the most commendable one

In experiments with dogs, heavily infected animals were considered poor risks for treatment, since large numbers of worms, if killed quickly and simultaneously may produce an embolus in the pulmonary artery and kill the dog. On the other hand, dogs (as well as cotton rats) with low initial microfilarial counts are unsatisfactory for assay purposes. These animals were used only in testing compounds which had shown activity in the cotton rat, in dosages derived from experience of their tolerance in cotton rats.

Three criteria were used in determining the effectiveness of new compounds against *Dirofilaria* in dogs, (1) a rapid and sustained reduction in microfilariae, (2) presence of dead worms in the terminal blood vessels within the lungs at autopsy, and (3) improved physical condition of the dogs.

Of 517 organic non-metallic compounds which were tested, several types showed activity in the cotton rat, but the best balance between activity and toxicity was found in the piperazines, administered orally or intraperitoneally. Detailed results of the effects produced by piperazine derivatives are presented in subsequent papers [see below]

J J C Buckley

HEWITT, R I, WHITE, E, WALLACE, W S, STEWART, H W, KUSHNER, S & SUBBAROW, Y. Experimental Chemotherapy of Filariasis. II Effect of Piperazine Derivatives against naturally acquired Filarial Infections in Cotton Rats and Dogs. *J Lab & Clin Med* 1947, Nov, v 32, No 11, 1304-13

The authors found that several members of the piperazine group produced precipitous reductions in the microfilarial counts in cotton rats after various oral or intraperitoneal doses. Of these derivatives, 1-carbethoxy-4-methylpiperazine hydrochloride (compound 180-C) was consistently effective and was at first used as standard in the treatment of 81 cotton rats. Detailed results of this series are tabulated. Compound 180-C was markedly effective against microfilariae in cotton rats in well tolerated doses but its effect against adult worms was not as promising. In dogs, the dosages which reduced microfilariae had adverse effects on the dogs themselves. However, another compound 1-diethylcarbamyl-4-methylpiperazine hydrochloride (84-L) was subsequently chosen as standard, and was effective in reducing microfilariae in doses as low as 3 mgm per kilogram in cotton rats, and produced no toxic effects in dogs, in therapeutic doses. Furthermore, frequent administration of compound 84-L resulted in the death of a large proportion of adult worms in cotton rats.

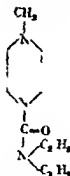
A detailed report on this compound is given in another paper in this series [see below]

J J C Buckley

HEWITT, R I, KUSHNER, S, STEWART, H W, WHITE, E, WALLACE, W S & SUBBAROW, Y. Experimental Chemotherapy of Filariasis. III Effect of 1-Diethylcarbamyl-4-Methylpiperazine Hydrochloride against naturally acquired Filarial Infections in Cotton Rats and Dogs. *J Lab & Clin Med* 1947, Nov, v 32, No 11, 1314-29

Detailed data are presented showing the effects produced by 1-diethylcarbamyl-4-methylpiperazine hydrochloride (compound 84-L) on

natural infections with filarial worms of cotton rats and dogs. The structural formula of compound 84-L is given below —



Two hundred and twelve cotton rats and twenty five dogs were used in testing this compound against both the microfilariae and the adult filariae. After oral or intraperitoneal treatment of filaria infected cotton rats at doses ranging from 3 to 100 mgm. per kilogram the microfilarial count dropped suddenly within 24 hours and became negative or remained very low as long as treatment continued. *In vivo* experiments led to the conclusion that the compound acts directly on the microfilariae in the blood. The rate of disappearance of microfilariae in dogs is not so rapid as in cotton rats but in one to two weeks over 90 per cent. generally disappear.

The effect of the compound on adult filariae in cotton rats varied with (1) the amount of drug given, (2) the frequency of the dosage and (3) the number of days lapsing from cessation of treatment to autopsy. Of 150 rats treated with 10 mgm. per kilogram at least twice daily 72 per cent. showed either some or all adults dead at autopsy but dosage three times daily was shown to give more consistent results.

In general animals treated with less than 10 mgm. per kilogram did not exhibit as many dead worms at autopsy as those treated with 10 mgm. or more per kilogram. Usually the longer the period between cessation of treatment and autopsy the fewer live worms were found on autopsy. Oral and intraperitoneal treatment of dogs with compound 84-L was encouraging in that doses necessary to affect the microfilarial counts and in some cases, to affect the adult worms, did not produce signs of severe toxicity. Detailed data of the results of treatment of 25 filaria infected dogs are tabulated. Although the optimum treatment schedule has not yet been determined it appears that frequent administration of the drug for several weeks is desirable.

J J C Buckley

VAN HOUT L. HENRIARD C. PIERI E & WANSOV M. Sur la chimiothérapie de l'Onchocercose (Note préliminaire): The Chemotherapy of Onchocerciasis: Preliminary Note. *A Soc Belg de Méd T p.* 1947 Mar 31 v 27 No 1 173-7

Since 1944 the authors have systematically tested various drugs for curative action in onchocerciasis — oil of chenopodium, eucalyptus, thymol, commercial pyrethrum, antimonials, atarsin and Trypanosan. Only the last gave indication of usefulness and its effect was transient. This, however, encouraged the authors to try the organic trypanocidal drugs especially Antirypol (or Belganyl). In 1942, moreover 14 volunteers for (successful) experimental infection with *O. volvulus* also volunteered for infection with trypanosomes and were treated

with Antrypol, more than two years afterwards they were found free, not only from trypanosomiasis, but also from onchocerciasis

The authors have treated with Belganyl a series of patients suffering from onchocerciasis. At first they gave two doses, each of 2 grammes, each week, but after the second or third injection there was often an intense reaction, with fever, severe articular pains, pruritus about the skin lesions, and massive exfoliation, and pain in the onchocercal tumours. Patients with eye involvement showed conjunctival reactions. Later the authors found that a total dose of 7 grammes, given at the rate of 1 gramme each week, was usually enough to cause disappearance of microfilariae and macrofilariae within 1-2 months, a total dose of 10 grammes appeared always to be successful. Dead adult filariae, containing dead and degenerated embryos, are found in the tumours. The authors found appreciable amounts of the drug in cysts, even 6 months after the last injection.

Fuller details of this work are to be published later

Charles Wilcocks

STRYKER, W. A. The Intestinal Phase of Human Trichinosis. *Amer J Path* 1947, Sept, v 23, No 5, 819-27, 4 figs on 2 pls [27 refs]

There are few records of the discovery of adult *Trichinella spiralis* in the intestine of man. The author gives 7 of these. A few of them are confirmed by microscopical examination. Persistence of adult *Trichinella* in this situation has been recorded for 30 days, but not longer. Work on trichiniasis of experimental animals, especially that done by ROTH (*J Parasitology*, 1938, v 24, 225), suggests, however, that the female *Trichinella* produces larvae for about 6 weeks.

The author reports on a man, aged 35, who had acquired trichiniasis from raw pork sausage prepared from a hog raised and butchered by himself. Other members of his family were also infected and his daughter, aged 8, died. The patient's wife and the family doctor said that raw pork had been eaten once only, the father and daughter having eaten more than the others did.

The father had diarrhoea, marked muscular pain, fever and terminal respiratory distress. There were physical and electrocardiographic signs of myocardial damage and neurological abnormalities which suggested cerebral damage. Death occurred 54 days after eating the pork. Adult male and female *Trichinella* were found microscopically in many sections of both the large and small intestine, being more numerous in unopened portions of the intestine, whose contents were not disturbed. Most of the females contained larvae. The nematodes were free in the lumen or embedded in the mucosa, one having penetrated as far as the *muscularis mucosae*, though none penetrated further than this. Often one end was in the mucosa, the remainder projecting into the lumen. Most often the "uterine area" of the *Trichinella* was embedded in or in contact with the mucosa which showed no significant cellular reaction around the worms, lymphocytes or plasma cells and eosinophils being found elsewhere in the mucosa at a distance from the worms and also in control cases not infected with *Trichinella*. In the intestine granulomatous infiltration, haemorrhage or foci of necrosis were not found, but the infestation of skeletal muscles was unusually heavy, larvae being present even in the cremaster muscle of the spermatic cord. Single muscle fibres contained as many as 3 larvae at the level of a single section. Some larvae were still straight, but most were coiled and cyst formation had begun. Many muscle fibres showed hyaline degeneration and between them there was a heavy cellular infiltration of mononuclear macrophages, lymphocytes, plasma cells and many eosinophils. A few foci were purulent. Dr S. E. Gould found 2,677 larvae per gramme of diaphragmatic muscle, which is one of the heaviest infestations known. The

heart and brain showed typical trichinosis myocarditis and encephalitis, larvae being found in both these situations. Photomicrographs illustrate this.

The author briefly discusses the resistance of various hosts to *T. spiralis*, suggesting that man is relatively susceptible and that the intestinal phase of the first infection may be prolonged, because there is no acquired resistance and that infection with relatively large numbers of larvae may also prolong the intestinal phase. These were features of the case reported and they are correlated with the fact that the period of persistence of the adults in the intestine was one of the longest ever reported and larvae were still being released 54 days after infection. Persistence of the intestinal phase means persistence of the myocarditis and increased severity and duration of the myocarditis and encephalitis death during the acute phase being usually due to lesions of the heart and central nervous system. These organs are affected only by migrating larvae which do not encyst in them so that inflammation of these organs subsides when the larvae move on. Thus in the case reported, larvae were found in the heart and brain, in both of which there was granulomatous infiltration.

Attempts to remove the worms from the intestine are therefore important. The author thinks anthelmintics are of little use and recommends (with references to the literature) purgation, attention to the patient's fluid balance and general condition and administration of immune and convalescent sera which may affect the larvae and reduce the number of adults. *G. Lapage*

## DEFICIENCY DISEASES

HANAFY M. The Subacute Subnutritional Syndrome in Infants. *J. Roy Egyptian Med Ass.* 1947 Sept v 30 No. 9 440-50 18 figs. on pls.

Malnutrition in infants may present numerous different clinical pictures. The author believes that these are all stages in the development of a single syndrome. This conclusion is based on the study of 197 cases, mostly between the ages of one and three years all of whom had been fed for some months on a diet consisting only of rice or cereal water.

Four grades of severity are distinguished.

1. Weight loss up to 15 per cent. with or without signs of riboflavin deficiency.
2. Weight loss from 15 to 30 per cent. with irritability, diminished reflexes, and a dry inelastic skin. Oedema may be present.
3. Weight loss from 30 to 50 per cent. In some cases there are pellagrous skin lesions, in others an enlarged tender liver (pre-ascitic stage of cirrhosis).
4. Weight loss more than 50 per cent. Cirrhosis of the liver may be present with or without pellagrous lesions.

Only the more severe grades are described in detail. The picture corresponds closely to that of kwashiorkor in West Africa or infantile pellagra in South Africa. Some additional features were found. Bronchectasis was present in 5 per cent of cases. Carpopedal paresthesia suggestive of rickets was sometimes observed, although the blood calcium did not fall below 8 mgm. per cent. In some cases the bones showed a definite clinical picture of rickets. The stools sometimes contained blood, pus and mucus. Three cases resembled Von Jaksch syndrome with pleuromegaly, leucocytosis and anaemia.

Early cases responded to treatment with high protein diet and vitamins. In the more severe grades, nicotinic acid and vitamin B were ineffective.

In agreement with the observations of GILLMAN [this *Bulletin*, 1946 v 43, 237] administration of one factor alone made the general condition worse. Good results were obtained with vitamin B complex (the form is not stated) and with crude liver extract and best of all with these two together. Parathyroid hormone, first tried because of tetany, was also found to enhance the action of liver extract.

No figures of mortality rate are given, and little is said of prognosis except for the important point that the prognosis is not affected by the presence or extent of either oedema or pellagrous skin lesions.

Analysis of the symptoms and of the response to treatment suggests that the disease is the result of a multiple deficiency—of protein, vitamin B complex, and vitamins A, C, and D. To these may perhaps be added deficiency of unidentified factors present in liver extract. In late cases there may be a change in endocrine function, which can only be restored by replacement therapy with hormones.

[This paper is illustrated by many striking photographs. It is the first description of the kwashiorkor syndrome that has appeared from Egypt as such; it is important in view of the earlier suggestion that the disease occurs only in children of negro stock. In Egyptians, the syndrome appears to be unusually well-developed, covering almost the whole range of known deficiency states, since in some cases there was evidence of rickets and of vitamin A deficiency. These conditions are not part of kwashiorkor as it occurs in the tropics although they were present in some cases described by Gil in Mexico.]

In kwashiorkor the liver is typically fatty. Dr Hanafy's mention of cirrhosis with ascites raises interesting speculations. It is to be hoped that the results of post-mortem examinations will be published.]

J C Waterlow

GLUSMAN M. The Syndrome of " Burning Feet " (Nutritional Metalgia) as a Manifestation of Nutritional Deficiency. *Amer J Med* 1947 Aug v 3 No 2 211-23 [50 refs.]

HO, T T. Een klinische observatie omtrent beri-beri onder het werkvolk in Tandjong-Priok in de Japanse bezettingstijd. [Clinical Beri-beri in Batavia Port during the Japanese Occupation.] *Med Maandblad* 1947, Dec, No 17, 326-31. English summary.

This investigation relates to the examination of 1,000 recruits for work in the harbour of Batavia and not to applicants for admission to hospital. Already this labour population, after 9 to 12 months of Japanese occupation, showed bodily deterioration. Out of the thousand coolies examined 157 were found suffering from severe beri-beri with serious cardiovascular symptoms, and large numbers suffered from slighter degrees. It was especially noteworthy, and by previous standards the reverse of expectation, that 150 out of the 157 showed dry beri-beri and only 7 wet beri-beri. This leads the author to ask whether dry beri-beri is not explainable as a partial thiamin deficiency and whether there is present in thiamin an anti-oedema factor. The clinical signs of dry beri-beri are given in detail and it was noted that the calf muscles were neither swollen nor painful, reflexes were heightened, there might even be clonus, and the patellar and tendo achillis reflexes were especially marked. Rapid response to treatment with thiamin is illustrated by reference to 14 specially selected cases.

A general summary of the deductions made is presented as follows. In place of the classical beri-beri triad of (1) oedema, (2) heart and vessel symptoms, (3) polyneuritic degeneration, the author gives the following description—

Anewin-deficiency leads to degenerative changes of peripheral nerve twigs, chiefly restricted to two regions, those of (a) the peroneal nerve and the tibial nerve (b) the vagus nerve and vasomotor twigs. The predominance of the lesions in one or other or both of these two regions represents the clinical distinction between wet and dry beriberi."

W. F. Harvey

## SPRUE

FOURMAN L. P. R. The Chylomicron Count in Normal Subjects and Patients with Sprue. *Trans. Roy Soc Trop Med & Hyg* 1948, Jan., v 41 No. 4 537-44 [10 refs.]

After a fatty meal, the serum has a characteristic milky appearance, and under dark-ground illumination numerous fine particles less than  $1\mu$  in diameter are seen in a state of Brownian movement. These chylomicrons consist of neutral fat with an outer layer of globulin. Particle counts are made on a small drop of serum spread out by pressure between slide and coverslip. They are estimated in terms of the number of particles per standard field.

In an investigation on fat absorption in sprue, counts were made before and after a meal of 200 ml. of homogenized evaporated milk containing 18 gm. of fat. Chylomicron counts in individual cases were compared with the percentage fat absorption on a controlled diet and with blood fat and glucose tolerance curves. Eighty-seven curves were constructed on data from 28 patients with sprue and these were compared with eighteen curves on seven normal subjects. With a meal containing 18 gm. of fat the peak counts in normal persons ranged between 100 and 270 particles per standard field. The chylomicron curve in normal persons increased and diminished when more or less fat was given, suggesting that they do at least represent one form of absorbed fat. On the other hand, low curves were produced in normal persons by giving calcium lactate with the meal. In fat balance experiments calcium lactate did not produce steatorrhoea. When flat chylomicron curves returned to normal with clinical improvement there was no corresponding diminution in the steatorrhoea. Chylomicrons were shown to represent a variable fraction of the absorbed neutral fat in the serum. In untreated sprue low curves were found in about half the patients examined. After 2 or 3 weeks of parenteral liver therapy patients whose curves had been low gave normal curves.

It is concluded that a small proportion of the total fat is absorbed without splitting as finely emulsified fat.

Whilst all patients with sprue have a defective absorption of split fat only some show impaired neutral fat absorption as judged by the chylomicron count. Failure to absorb neutral fat is more common in the severe cases and responds to liver therapy.

P. MARION-BABE

SPIEL, T. D., GARCIA, L., PELI, G., STONE, R. E., MILANES, F., BRANDENBURG, R. O. & ARAMBURU, T. Further Observations on the Specificity of the Folic Acid Molecule. *Blood* 1948 Jan. 3 No. 1 121-8 9 figs.

Methyl folic acid, N-(4-(4-quinazolinyl)amino)benzoic- $\beta$ -glutamic acid, the Mg salt of formyl pteroyl glutamic acid, the Mg salt of formyl pteron acid, pteroyl aspartic acid, oxyfolic acid and pteronic acid has been studied as to their effect on blood regeneration in selected cases of Addisonian pernicious anemia, nutritional macrocytic anemia and tropical pruritus. In the amounts administered only the Mg salt of formyl pteroyl glutamic acid was effective.

in producing reticulocytosis and an increase in red blood cells, hemoglobin, white blood cells and platelets and it was not as effective per unit of weight as was folic acid per se. Presumably this compound is slowly changed into folic acid in the body. It is of special interest that the Mg salt of formyl pterotic acid (*Streptococcus lactis* factor) was negative in producing hemopoiesis. These observations show the very great specificity of the folic acid molecule.

DARBY, W. J., JONES, E. WARDEN, H. F. & KASER, Margaret M. The Influence of Pteroylglutamic Acid (a Member of the Vitamin M Group) on Gastrointestinal Defects in Sprue. A Study of Interrelationships of Dietary Essentials. *J. Nutrition* 1947 Dec 10 v 34, No 6 645-60, 5 figs (1 coloured) [43 refs]

Patients with the complete sprue syndrome may exhibit remarkable combinations of deficiency states. Some of these manifestations are: loss of weight (caloric deficiency), hypoproteinaemia (protein deficiency), petechiae (vitamin K or C deficiency), night blindness and xerosis conjunctivae (vitamin A deficiency), hypocalcaemic tetany and osteoporosis (vitamin D and calcium deficiency), and pancytopenia (vitamin M deficiency). In many cases these deficiencies may be classified as latent or potential.

With the demonstration of the activity of pteroylglutamic acid (PGA) [folic acid] in sprue patients it has been indicated that this vitamin exerts a favourable influence upon the gastro-intestinal abnormalities as well as upon the anemia. In this paper additional evidence is adduced that PGA does so.

Six adult patients were under observation and all demonstrated the diagnostic criteria. The sole specific drug administered was synthetic PGA in doses of 5 mgm daily by the mouth or 15 mgm intramuscularly except in one patient in whom this was preceded by 10 days' therapy with pteroylglutamate. During treatment one was on a milk-free diet but the remainder were on a regular ward diet.

During each relapse the patients complained of glossitis and all showed atrophy of lingual papillae. Subjective relief of glossitis resulted and the commencement of regeneration of papillae was evident within 3 days to one week. In relapse the same succession of events took place. If the appearance of the tongue is an indication of the state of the gastro-intestinal tract then it can be inferred that this vitamin exerts the same beneficial action on the mucosa.

In all remissions cessation of diarrhoea was observed within a period of 3-9 days from the beginning of PGA therapy.

The minimum gain in weight varied from 6 to 45 pounds. The impression gained is that the weight changes were the result of increased appetite and better absorptive capacity of the gastro-intestinal tract.

A typical blood picture (oral administration) there was a definite return to within the normal type of curve within 11 to 30 days after the institution of therapy. It is permissible to suggest that PGA assists the permeability of the gastro-intestinal tract.

The control of fat intake of patients is difficult. Observations on the effect of PGA on fat tolerance were limited by successive determination on a large patient load. In a few cases the 24-hour loss of fat in the stool was determined. The results are of doubtful value but do not extend that obtained in the other patients.

A series of experiments with PGA have already been reported. The present study was designed to determine the effect of PGA on the absorption of various nutrients. The results are of doubtful value but do not extend that obtained in the other patients.

Vitamin A absorption determinations after an oral dose of 200,000 I.U. have shown that improved absorption had taken place in 2 out of 4 remissions studied. The hypoprothrombinaemia in sprue is attributed to deficiency of vitamin K. Two patients with hypoprothrombinaemia, before PGA therapy became normal during remissions.

The decrease in serum tocopherol (vitamin E) concentration during a sprue relapse as well as an increase after PGA administration are shown by graphs. There is a contrast between concentrations of fat-soluble vitamin E in patients with sprue and in those with pernicious anaemia.

X-ray changes of the so-called deficiency pattern type are present in sprue. In 3 out of 4 follow up films in remissions induced by PGA, a definite improvement in the pattern occurred.

The observations may be interpreted as indicating that the primary defect in sprue is a deficiency state which is corrected by PGA. The numerous interrelationships of PGA with other vitamins and food factors are a remarkable clinical example of similar relationships of foodstuffs in man and closely resemble the multiple deficiency states in the sulphonamide-treated rat.

As many cases of chronic sprue undoubtedly develop irreversible changes in the gastro-intestinal tract, and as degenerative changes in the intrinsic nerve plexuses have been demonstrated, it is improbable that they can be restored. Therefore the persistence of some degree of malfunction may be expected despite therapy.

Any disease which produces malabsorption from the gastro-intestinal tract may resemble the sprue syndrome and it is to be expected that PGA will be ineffective in the treatment of any disease which does not result from a deficiency of this vitamin. This factor should enable clinicians to separate the different clinical conditions which are loosely grouped together as the sprue syndrome. Regarding the possible synthesis of vitamins by the bacterial flora of the gastro-intestinal tract it has been observed that during PGA therapy a normal flora has been re-established in sprue. It is obvious that much more careful studies will be needed to define the relative rôles of altered gastro-intestinal absorption, metabolism and gastro-intestinal synthesis in the pathogenesis of the manifold deficiencies observed in sprue.

P. M. 100-Bahr

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## HEMATOLOGY

SPIES, T. D., GARCIA LOPEZ, G., STONE, R. E., MILA, E. S., F. TOCA, R. L. & ARAMBURG, T. Treatment of Nutritional Macrocytic Anemia with Synthetic Folic Acid. *Lancet*, 1948, Feb. 14, 236-41, 2 figs.

Two important advances have been made recently in the discovery that folic acid produces a prompt haemopoietic response in nutritional anaemia and that 5-methyl-tetraol (thymine) when given in several thousand times the dose produces a similar response. For the purposes of this study, 32 persons with nutritional macrocytic anaemia, all Europeans aged 35-70, the majority being males, were selected. In this arbitrary selection the following criteria were employed: the red cells were fewer than 3,000,000 per cmm., the bone marrow showed the typical erythroblastic arrest, repeated gastric analyses showed free hydrochloric acid in the gastric content, while the reticulocyte index was normal and no recent treatment had been given.



Rigid dietetic control in hospital consisted of the exclusion of meat, meat products, poultry and fish, while detailed histories showed that the diets of these patients had been grossly deficient in protein and the vitamin B complex for many years. All patients had lost weight and complained of tiredness and in all diarrhoea had been present from one to three months.

Pain, burning and sensitivity of mouth and tongue were common and many had paraesthesiae and hypoaesthesia. Oedema, associated with a reduction of serum-albumin was present in 9, pellagra, scurvy, riboflavin deficiency and aneurin and ascorbic acid deficiencies in others.

After folic acid treatment, reticulocytosis, increase in haemoglobin and in erythrocytes indicated a satisfactory response in every case. Follow-up studies for eighteen months have shown that none had a severe relapse. The response was adequate to 10 mgm of folic acid daily, which was continued in some patients for as long as 77 days. In contrast to patients with Addisonian pernicious anaemia, no evidence of development of subacute combined degeneration of the cord was obtained. The blood-levels were maintained for eighteen to twenty-four months with no other specific therapy.

P Manson-Bahr

COWAN, G A B. Folic Acid in Severe Nutritional Anaemia: a Report of Five Cases. *Trans Roy Soc Trop Med & Hyg* 1948, Jan, v 41, No 4, 525-35, 5 figs

Severe anaemia in Malaya is responsible for much ill-health and many deaths. The causes are malaria, helminthic infection, malnutrition and chronic infections. Out of 142 cases, 24 were found to have red-cell counts of less than one million per cmm. Analysis of these showed that nutritional macrocytic anaemia accounted for nine (three associated with pregnancy), dimorphic anaemia for fourteen and iron-deficient anaemia for one only.

A nutritional factor, apart from iron, was thus concerned in 23 cases, and five of these were treated with oral synthetic folic acid. The total folic acid given was from 160 to 560 mgm in from 16 to 42 doses. Reticulocytes reached their peak on about the 7th day of treatment. In each case the response to treatment was satisfactory: in two it was dramatic, both of these were examples of dimorphic anaemia.

P Manson-Bahr

## VENOMS AND ANTIVENENES

SERGEANT, Et. Sérothérapie antiscorpionique (dixième note). Observations médicales reçues pendant l'année 1946. [Anti-Scorpionic Serotherapy X Medical Reports received in 1946] *Arch Inst Pasteur d'Algérie* 1947, June, v 25, No 2, 94-7

During the year, 868 patients were treated, according to instructions, for scorpion sting: all survived except 4 of the group (124 in number) whose symptoms were alarming and in whom life was endangered. In addition there were 3 deaths in infants who were not treated, and 12 in persons treated with insufficient serum, or too late. The total figures since 1936 are 3,089 treated, of whom 655 showed grave symptoms, of these 655 patients, 592 (90.3 per cent) were cured.

The author points out that patients should be kept under observation for several hours after administration of the serum, even if the symptoms have disappeared, because occasionally the improvement is apparent only, and there

may be a return of symptoms, and death. Instructions are given that if symptoms are severe at least 20 cc. of serum should be injected, and repeated if there is no improvement in one hour and again, several times, if necessary. A return of symptoms indicates another injection.

The scorpions were identified in 39 cases—

- 23 *Pseudoscorpion*
- 11 *P. scorpion*
- 1 *P. pugnatrix*
- 4 *Buthus scorpion*

[See also this Bulletin, 1947 v 44 534-535.]

Charles H. Woods

SERGEANT ET. Intervalle de temps qui peut s'écouler entre l'injection de serum antiscorpionique et la sédation des symptômes d'envenimement. [The Time between Injection of Anti-Scorpionic Serum and Alleviation of Symptoms.] *Arch. Inst. Pasteur d'Algérie* 1947 June v 25 No. 2, 98-100, 1 graph.

A study of the symptoms of scorpion sting in 209 cases in which the patients condition was serious before injection of serum shows that alleviation of the local pain, vomiting and sweating occurred within one hour of the injection of serum in 45 per cent. In almost all cases the improvement was evident within 8 hours, though in a very few it was delayed even as long as 18 hours after the injection.

Charles H. Woods

## DERMATOLOGY AND FUNGI'S DISEASES

FAMBREMEGHEM R. Importance des affections dermatologiques chez les Européens au Congo Belge. [The Importance of Skin Diseases in Europeans in the Belgian Congo.] *Ann. Soc. Belges de M.d. T. p.* 1947 June 30 v 77 No. 2, 251-5

The author reviews the cases of skin affections found among a small European population of about 208 persons, residing in a fairly humid region of the lower Congo from December 1944 to December 1945.

By means of a graph showing monthly rainfall and the percentage of skin cases among his total consultations he demonstrated that skin diseases account for about 20 per cent. of the morbidity rate and are most prevalent in the rainy months.

Mycotic and pyrogenic affections comprise about 25 per cent. of the total.

C. C. Christensen

HADLER, W. A. Classificação do pénfigo foliaceo baseada em dados anatomicos clinicos e hematologicos. [Classification of Cases of Pemphigus foliaceus.] *Tratado de Dermat. e 5 filografia de São Paulo* 1947 Mar-June 11 Vol. 1/2, 29-56, 1 fig. & 1 graph 1 refs. English summary

Several classifications of this disease have been proposed—that of VIEIRA according to the course—hyperacute, acute, subacute and chronic—but the last is subdivided on a pathological basis into bullous, pustular, papulomatous, pigmented, herpetiform, i.e. that of RABELO into 3 clinical types—erythematous-exudative, herpetiform, and exfoliative bullous—that of OSMI into benign

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(*formes frustes*), with scattered lesions, or circumscribed (the Senear-Usher syndrome), and the severe generalized type, subdivided into herpetiform, exfoliating bullous and exfoliating pustular, lastly, that of TORRES into the bullous, the chronic or foliaceous, and the cachectic [see this *Bulletin*, 1945, v 42, 311]

The author proposes a new classification based on the results of blood examination, the clinical course and the histopathology of the skin lesions—a mingling of those cited above. The blood differences are given in a protocol of the averages of 16 *formes frustes* and 314 generalized cases. These differences are not great, the main being a higher eosinophila in the latter, 14.8 per cent as compared with 10.46 in a total leucocyte count of 10,469 and 9,282 respectively, and a differing "nuclear deviation" [? Arneth index], 1/22.5 in the *formes frustes*, 1/14.6 in the generalized type. The histology of the skin in the acute bullous phase, the chronic, the cachectic and retrogressive phases are well shown in a series of photomicrographs, and photographs of patients depict the clinical variations. The chronic phase, the author states, may be further subdivided into foliaceous, erythrodermic and pigmentary forms.

H Harold Scott

FONZARI, M. Doses de metoquina no tratamento do pênfigo foliaceo [The Dosage of Metoquine (Atebrin) in the Treatment of Pemphigus foliaceus] *Arquivos de Dermat e Sifilografia de São Paulo* 1947, Mar-June, v 11, Nos 1/2, 17-28. English summary

There has been considerable conflict of opinion as to the dosage of atebtrin and the length of time for which it can be given with safety, and what intervals should be interspersed when courses of it are administered.

The author has tried it in a large number of cases of *pemphigus foliaceus*. He started with 0.2 gm daily for a week, then, after the lapse of 4 days, repeated the course. Observing no ill effects, he tentatively increased the dose first to 0.3 gm, then to 0.4 and so on, even up to 1.0 gm and maintained it for several weeks, even months, and rarely did he observe untoward symptoms. One man, having had 0.2 gm daily, then 0.3 and finally 0.4 gm till he had had in all 29.4 gm did develop a "toxic psychosis" [not described]. Brief notes—a couple of lines or so to each—are given of 50-60 cases, several were given 80-90 gm in 7 months and one had 110.8 gm in 9 months. Some patients cleared up on this treatment, but commonly a few lesions remained, especially on the legs, and after cessation of treatment these might retrogress. It would appear that when the condition had so far improved as to leave only these few lesions, further treatment with atebtrin was ineffectual. The best results were observed in those who exhibited marked yellowing of the skin, this staining is not to be regarded as a toxic symptom and it clears up in time, whether treatment is continued or not. Other drugs such as paludrine and plasmoquine were tried but were quite ineffectual in this disease.

H Harold Scott

BASSET A. COLDEFY & DE KOUROCH. Trois cas parisiens de pied de Madura dus à une mycose (famille des *Aspergillacées*) [Three Cases of Madura Foot in Paris due to an Organism of the *Aspergillaceae* Family] *Bull Acad Nat Méd* 1948 v 132 Nos 1/2 41-4

DOSTROVSKY, A. & SAGHER, F. Failure of Sulphonamides and Penicillin in Maduromycosis. *Lancet* 1948 Jan 31, 177-8, 2 figs [15 refs]

The authors note that little attention has been paid to the effect of sulphonamides or penicillin on deep mycoses of the skin such references as are quoted refer largely to actinomycotic lesions, and such a one, in a case of Madura

foot, is referred to by PETERS [this Bulletin, 1946 v 43 46]. In Peters's case, 1,050,000 units of penicillin were given without specific effect.

The case described by the present authors was one of madurumycosis in a native of Aden. Colonies of a madurella type were found on culture and these resembled *Madurula americana*. Intracutaneous tests with trichophyton and with material from cultures of the lesion were negative. Therapy which included sulphapyridine (total dosage 72 gm.) brought about improvement, but not healing. Three and a half years later the patient was seen again, and there was now considerable involvement of the bones of the foot. Therapy included sulphadiazine (total dosage 100 gm.) and X rays. As this was without effect, sodium penicillin was given in intramuscular doses of 10,000 to 15,000 units every 3 or 4 hours to a daily total of 90,000 units in addition, injections of 10,000 units were given locally into the tumour. In 50 days a total of 5,000,000 units of penicillin was given. Secondary infection was overcome but the mycetoma did not respond and the foot was therefore amputated.

Practical difficulties made it impossible to test the sensitivity of the fungus to penicillin *in vitro*. The authors believe that the failure of penicillin may be explained by (1) insensitivity of the fungus (2) insufficient dosage (3) inadequate contact between the penicillin and the fungus, because of the depth in the bone to which the mycetoma had penetrated.

H. J. O'D. Burke-Gaffney

FRUSS & DELVOUTZ. A propos d'un aspect chirurgical d'une mycose rare histoplasmosse. [Concerning a Surgical Aspect of a Rare Mycosis; Histoplasmosis.] *Cahiers Méd. Union Française Algérie*. 1947 June v. No. 11 419-25 8 figs.

The authors describe a fatal case of histoplasmosis, of an unusual pathological type in a native of Senegal, in which the lesions occurred chiefly in the osseous and cutaneous systems. The upper cervical vertebrae were extensively damaged and a resulting cold abscess, pointing in the posterior triangle of the neck, prompted the diagnosis of Pott's caries of the cervical spine. "Gummatous lesions, in which the large parasitic form of *Histoplasma capsulatum* measuring up to 1.5  $\mu$  in diameter was found, occurred in the frontal and maxillary bones, the femur, the tibia and the bones of the forearm. *H. capsulatum* was cultivated from the lesions before and after death. The skin over the greater part of the body was thickened, dry and cracked in places, and milium ulcers were scattered on the face and limbs. Histological examination of the skin revealed hyperkeratosis of the epidermis with giant-cell granulomata, rich in *Histoplasma* in the cutis. Outstanding pathological features of this case were the unusual distribution of the lesions with apparently no involvement of the lymph nodes or the lungs and only minor involvement of the liver and spleen.

[This is only the fifth reported case of histoplasmosis from tropical and northern Africa: the other four were two diagnosed by the reviewer in 1943 and 1946 one by CATANEI & HERMAN in 1945 (this Bulletin 1946 v 43 77) and one by HERMAN & ARETAS in 1947 and 1948 v 45 207]. In all, the parasite was of an unusually large size measuring from 12 to 15  $\mu$  in largest diameter which suggests that there is a distinct African variety of *Histoplasma capsulatum*.  
J. T. Duncan

MILLER, H. E. KEDDIE, FRANCES M. JOHNSON & BOSTICK, W. L. Histoplasmosis: Cutaneous and Mucocutaneous Lesions, Mycologic and Pathologic Observations. *Arch. Dermat. & Syph.* 1947 Dec., v 56 No. 6 715-37 3 figs. (Refs in footnotes)

This is a general account of histoplasmosis compiled from the recent literature in which emphasis is specially placed on the mucosal and cutaneous lesions

which are of interest to dermatologists. The authors also describe, at great length, the clinical and pathological features of a case of this disease in which the only ascertained lesion of histoplasmosis was an ulcerating nodule, 1.5 cm in diameter, on the dorsal aspect of the tongue. The diagnosis was based on the identification of *Histoplasma capsulatum* in scrapings from the ulcer and on the isolation of the fungus from this material. There was general lymphadenopathy and some enlargement of the liver, but not of the spleen. A few bodies which may have been *Histoplasma* were seen in some of the cervical lymph nodes, but, on the whole, the microscopical examination of the lymph nodes yielded data more suggestive of Hodgkin's disease than of histoplasmosis. The final diagnosis, based on the necropsy findings, was generalized miliary tuberculosis, Hodgkin's disease of the malignant lymphoma type and localized histoplasmosis.

[It is noteworthy that cases have been described of histoplasmosis and of torulosis which bore a strong resemblance to Hodgkin's disease, not only in their clinical features but in the histology of the lymph nodes, and there is still uncertainty as to whether these were cases of true Hodgkin's disease with superadded mycosis, or the uncomplicated mycoses simulating Hodgkin's disease.]

J T Duncan

ROSENTHAL, S R & ROUTIEN, J B. Contagiousness of Coccidioidomycosis. An Experimental Study. *Arch Intern Med* 1947, Sept, v 80, No 3, 343-57, 5 figs [Refs in footnotes]

Infection in coccidioidomycosis is caused by inhalation of the air-borne spores of the saprophytic growth of *Coccidioides immitis*, and the disease is not known to be transmitted directly from man to man. The work recorded in the present paper was designed to explore the possibility of direct transmission of the infection by transference of the parasitic spherules of the fungus. Experimental infection of guinea pigs was accomplished by intratracheal insufflation of sputum, pus, ground-up granulation tissue or lymph node material, containing the parasitic spherules, from human sources. The infective material was introduced through a wide-bore syringe needle inserted into a tracheotomy opening, and it was driven into the bronchial tree by air pumped from the syringe. The resulting lesions of coccidioidomycosis were found chiefly in the upper lobes of the lungs. Infection was also effected by intraperitoneal injection of similar materials. As a test of survival of the parasitic form of the fungus outside the body, morbid materials containing the spherules were stored for varying periods at 12°C. These materials were found to be infective to the guinea pig by intratracheal insufflation up to 110 days.

From the results of their experiments, the authors conclude that coccidioidomycosis should be considered to be contagious until the contrary is proved.

J T Duncan

McLAUGHLIN, F W. Coccidioidal Infection. *Bull U S Army Med Dept* 1948, Feb, v 8, No 2, 124-7.

Coccidioidomycosis is endemic in the Camp Roberts area in California and since the inception of the U S Army Hospital there in 1941, over 750 cases of *C immitis* infection have been confirmed [this *Bulletin*, 1946, v 43, 778].

The present author reviews 20 of these cases and notes that the usual symptoms were chest pain (20), fever (18) and cough (15). The commonest signs were X-ray evidence of pulmonary infiltration (20), increased sedimentation rate (12) and leucocytosis (8). Hilar adenopathy and pleural effusion were each seen once.

It is noteworthy that only 4 of the cases had positive skin tests and the author stresses the point that these tests are negative in many active cases of

coccidioidomycosis. Skin tests may however become positive very rapidly and a detailed account is given of one patient on whom such a test was positive at 1/1,000 on the fifth day after mild symptoms were noticed. On the other hand, complement fixation and precipitin tests do not always become positive early—a case is quoted of a patient having X-ray evidence of a chest lesion and showing a positive skin test at 1/1,000 but whose complement fixation did not appear for over 3 weeks.

The two serological tests are usually necessary for final diagnosis, since lesions seen in chest films so closely resembled those of tuberculosis. In many cases skin tests for tuberculosis and for coccidioidomycosis were both positive and indeed occasionally the two diseases may co-exist.

The best method of diagnosis is probably obtained by culture of sputum and guinea-pig inoculation, where facilities are available. The author found the raised sedimentation level to be fairly frequent (the figure of 60 per cent. is given but the numbers were only 17 out of 20). He also believes the sedimentation rate to be of prognostic significance especially since its return to normal tends to correspond with X-ray evidence of clearing. It is suggested that the sedimentation level is an important factor in determining when a patient may become ambulatory (as in the case of rheumatic fever).

No specific therapy was found and penicillin and sulphonamides proved ineffectual. Treatment was largely a matter of general principles and good nursing.

H J O'D Burke-Gaffney

## MISCELLANEOUS DISEASES

RAYMOND W D Notes on a Poisonous East African Species of Wild Cucumber (*Cucumis aculeatus*) East African Med J 1947 Dec. v. 4 No. 12, 450-51

The toxicity of a number of species of wild cucumber has been investigated in South Africa—it has been shown that *Cucumis africanus* and other species contain a toxic principle cucumin, which is neither a glycoside nor an alkaloid. In human poisoning violent diarrhoea has been noted. In laboratory animals, postmortem appearances varied with the dose—with small doses, the gastrointestinal tract was principally affected—with large doses, pulmonary oedema was the usual cause of death.

The author describes a fatal case of poisoning of an African in Tanganyika who was treated for headache by a local medicine man with the fruit of a plant *Asarum*—this was identified as *Cucumis aculeatus*. Vomiting and diarrhoea occurred soon after the medicine was taken. Death took place within 8 hours and although the passage of time during transport obscured the autopsy findings, pleural adhesions were noted.

From the fruits a substance was isolated which gave reactions similar to those described for cucumin—it is highly probable that the fruit contains a substance closely related to if not identical with cucumin.

The substance isolated and fresh extracts of the fruit were lethal, within 1 to 8 hours to a mouse, two white rat and frog, on injection. In the rats and the mouse dyspnoea and cyanosis were noted and the pathological findings in the lungs at postmortem showed that they had the appearance one would find in acute pulmonary oedema.

Other local species of *Cucumis* known to be poisonous are *C. ficusoides*, *C. ficiformis* and *C. auratus*—poisoning has also occurred from other species not exactly identified botanically.

H J O'D Burke-Gaffney

- DONOSO BARROS, R Myiasis humana en Chile Consideraciones clinicas y epidemiologicas [Human Myiasis in Chile Clinical and Epidemiological Features] *Rev Chilena de Hig y Med Preventiva* 1947, Mar, v 9, No 1, 3-59, 3 figs & 10 pls [83 refs]

The author bases his remarks on 112 cases of human myiasis under his personal observation during the five years ending 1946. The numbers in successive years were 1, 2, 7, 17 and 85, 7 were under 5 years of age, 10 each between 36 and 40, and 46 and 50 years. His own observations are supplemented by references to and quotations from the literature and there is a very full bibliography. The author divides his cases into two main groups. Myiasis of cavities (*i.e.*, orifices), nasal, aural, ocular, vulvovaginal and intestinal (including the mouth). The second group is that of cutaneous myiasis, attacking the unbroken skin or lesions such as ulcers, wounds, etc. The following larvae were identified: *Cochliomyia hominivorax*, *Calliphora erythrocephala*, *Musca domestica*, *Musca chilensis*, *Fannia canicularis*, *Eristalis tenax*, *Oestrus ovis*, *Gastrophilus veterinus*, *Sarcophaga carnaria* and *Parasarcophaga barbata* [*Sarcophaga barbata*]. In previous accounts *C. macellaria* has been named as causing myiasis in Chile, but this, it is stated, was a mistake for *C. hominivorax* [though some authors use the names as synonyms]. *H. Harold Scott*

- MILLER, J M & THOMISON, S J Surgical Aspect of Infestation with Intestinal Parasites *Southern Med J* 1948, Feb, v 41, No 2, 178-80

"Case reports of patients with *Enterobius vermicularis*, *Schistosoma japonicum*, hookworm, and amebiasis have been presented. The discovery of parasites in patients with otherwise unexplained abdominal symptoms will remove this group of individuals from those with the unsatisfactory diagnosis, 'abdominal pain, cause undetermined'. The surgeon is urged to familiarize himself at least superficially with these parasites, that he may consider them in his differential diagnosis of unusual abdominal pain."

## PROTOZOOLOGY GENERAL

- APPELBAUM, A Human Toxoplasmosis Report of a Case in an Adult with Ocular Manifestations *Ann Western Med & Surgery* 1947, Oct, v 1, No 8, 323-32 [27 refs]

The paper describes a case of toxoplasmosis in a white man 30 years of age and gives a general summary of the literature of the subject. The case in question was examined because of the patient's complaint of blurred vision of the left eye, a small patch of chorio-retinal atrophy was found just temporal to the fovea centralis, together with a small recent haemorrhage between the patch and the fovea centralis. Two years later the patient was again examined and he now revealed a bilateral central chorio-retinitis. The lesion in the left eye had increased in size and showed a black pigmented centre and a zone of peripheral pigment. In addition, two other small lesions had appeared. As toxoplasmosis was suspected, a serological test for neutralizing antibodies was carried out. This was positive. Cerebrospinal fluid injected into mice did not give rise to infection. The author points out that this case is the forty-second to be reported in the U S A since 1939. Of these cases, nine occurred in persons over 15 years of age.

*C M Wenyon*

KRAY B. H. & GRACUTT R. G. Asymptomatic Toxoplasmosis. *Am J Trop Med.* 1947 Nov v 27 No. 6 45-8, 1 fig. (17 refs.)

A man 29 years of age died from an accident, and examination of sections of the heart muscles revealed a cyst measuring 34 by 98  $\mu$ . It was filled with spores, 250 being countable in the section. There was no inflammatory reaction round the cyst. Extensive examination of further sections from the heart and other organs failed to reveal any other parasites. It is thought that the cyst shown in a microphotograph represents a toxoplasma. C. M. Warren

## ENTOMOLOGY AND INSECTICIDES GENERAL

LIMSDEN W. H. R. Observations on the Effect of Microclimate on biting by *Aedes aegypti* (L.) (Dipt., culicid.) *J Exper Biol.* 1947 Dec v 4 Nos. 3 & 4 381-73 2 figs. (23 refs.)

The mosquitoes were reared under carefully controlled conditions, and were offered a blood meal in a small cage applied to the human arm in darkness. It was found that wide variations of the relative humidity did not appreciably affect the proportion biting, which rose from about 10-20 per cent. at 10 C. to a maximum of 80 per cent. (within five minutes) at 35 C. Only about 60-70 per cent. fed at 40 C. Measurements of temperature gradients near the human skin were made with a sensitive electrical thermometer. At air temperatures below that of the skin, the gradient extended away for only about 1 cm. in nearly still air. At air temperatures above the skin there was a gentle reversed gradient for 2-3 cm. It seems unlikely that these gradients can be responsible for attracting mosquitoes to bite, especially when the air temperature is above that of the skin.

Dissections showed that in the majority of fed mosquitoes, blood was found in the stomach alone, but in partly fed mosquitoes there was a somewhat larger minority with blood in the diverticula also, probably because of regurgitation when feeding was interrupted. J. R. Hunter

PAREOT L. & DURAND-DELAURE, H. Notes sur les phlébotomes. LVII. Présence en Algérie de *Phlebotomus cf. des Sertan*, 1928. Notes on *Phlebotomus* LVII. Presence of *Phlebotomus cf. des Sertan* in Algeria. *Arch I st. Pasteur & Algine* 1947 Sept. Dec v 5 Nos. 3 & 4 10-11

SWELLENGREBEL, N. H. LODEN, J. G. & SWELLENGREBEL, J. M. H. Rapport over proven roepers beschikkingen van onderzoekingen omtrent DDT in Tjandjoer en omgeving. [Trial of DDT "Foliar Spraying" at Indonesian Dwellings.] *Med Maandblad. Batavia* 1947 Dec v 17 319-21

SCHMITZ, W. R. & GOETTLE, Mary B. Penetration of DDT into Wood Surfaces. *Soap* New York 1948, Jan. v 24 No. 1 118-21 2 figs.

Two types of DDT spray were used: kerosene solutions and aqueous emulsions of DDT dissolved in various solvents. The liquids were carefully sprayed on to strips of wood with an atomizer and the penetration was subsequently judged by extraction and chemical (chromatographic) estimation of DDT from layers scraped off the surface. The thicknesses of the layers of peeling were estimated by a craze micrometer measurements.

The authors used a variety of woods and the average recovery of DDT (kerosene solutions) from the first 0.001 inch was 5 per cent., and from the



first 0.006 inch 52 per cent, of the amount theoretically applied. Equivalent figures for emulsions, were 37 and 70 per cent respectively. At depths below 0.006 inch the amounts in different layers fell away asymptotically (Thus, at 0.04 inch the quantities recovered were still only 65-85 per cent.)

There was little evidence of correlation between the physical properties of the different woods and the recovery of DDT from the upper layers. Preliminary spraying of wood with water did not greatly improve DDT recovery if the DDT liquid was sprayed on immediately afterwards, but there was definite improvement after one spraying with water and drying for fifteen minutes before application of the DDT.

Tests with different solvents in the emulsion formula suggested that the more volatile DDT solvents tended to leave more DDT near the surface.

J. R. Busvine

SMITH, M. S. **Persistence of DDT and Benzene Hexachloride in Soil** [Correspondence] *Nature* 1948 Feb 14 246

## REPORTS, SURVEYS AND MISCELLANEOUS PAPERS

BULL. MÉD. DE L'AFRIQUE OCCIDENTALE FRANÇAISE 1946, v. 3, No. 2, 271-84. L'actualité médicale dans l'Ouest Africain. Conférence médicale Franco-Britannique d'Accra—Novembre 1946 [Franco-British Medical Conference, Accra, 1946].

The agreements reached at this Conference are set out *seriatim*. They cover — A. Cooperation between health services in the various countries of West Africa, and proposals for coordination of medical action, B. Agreements relating to the medical instruction of Africans, C. Facilities for the diagnosis of yellow fever (the accredited laboratories are at Dakar, Freetown, Accra, Lagos, Douala, Stanleyville, Brazzaville), D. Preparation and distribution of vaccines for mutual assistance, E. Collaboration in studies of nutrition, F. General principles of closer cooperation between the various countries, G. Final recommendations, in which it is noted that Belgian and other representatives agreed to the principal resolutions.

There are three Annexures, dealing respectively with mobile medical organizations, schedules of instruction for Africans, and the organizations interested in nutrition.

No adequate summary of this Conference can be given, the resolutions are given with little comment, and should be studied in the original. There is evidence of a desire to improve inter-territorial medical collaboration.

Charles Wilcocks

MALAYA. **Annual Report of the Institute for Medical Research, Malaya, for the Year 1946** [LEWTHWAITE R., Director] 52 pp 1947. Kuala Lumpur. Malayan Union Govt. Press. [\$1 or 2s 4d.]

In the introductory part of this Report, Lewthwaite briefly traces the history of the Institute since its foundation in 1900. He gives an account of the action taken just before the Japanese occupation, and in more detail, after the capitulation of the Japanese in 1945. The loss of equipment during the occupation was almost complete, and the laboratories were re-equipped from whatever sources could be tapped.

The demand for vaccines after the war was very great and was met with difficulty supplies were also needed for Siam and Borneo.

The author pays tribute to his colleagues not only for their scientific work in peace but also for their service in war several lost their lives and many of them suffered severely.

Work is now continuing as routine investigation or special research, in the Divisions of Bacteriology, Chemistry, Entomology, Malaria Research, Nutrition, Pathology and Serology and the branch laboratory at Ipoh is once more functioning. Records of these activities are displayed in the report.

Charles Wilecks

NEW ZEALAND WESTERN SAMOA. Twenty-Fourth Report of the Administration of the Territory of Western Samoa for Year ended 31st March, 1947 [VOELCKER, F. W.] 27 pp. Wellington Govt. Printer

Western Samoa comprises two large and several small, mountainous, islands. The climate is mild and equable the mean daily maximum temperature being 84.75°F minimum 73.82°F and the average annual rainfall 111 inches. The population consists of 15,765 non-Samoans and 65,685 Samoans most of the latter live in coastal villages. The islands are administered by the Government of New Zealand under the international trusteeship system of the United Nations, but their status is under review.

The medical section of this Report (p. 19-23) is brief. The staff consists of 3 European medical officers, 22 Native medical practitioners, 7 Native dental officers, 1 qualified bacteriologist of part-Samoan descent, 11 European nursing sisters, 97 Native nurses, and others. There is a considerable hospital at Apia, which accommodates Europeans, Samoans and Chinese and includes a laboratory and X-ray department. There are 13 medical out-stations to each of which a Native medical practitioner and nurse are attached. At all stations, in 1946 there were 3,631 in-patients and 99,104 out-patients.

The principal infective diseases reported in 1946 were tuberculosis (49 cases), malignant jaundice [not otherwise defined] (71), catarrhal jaundice (93), pneumonia (244), bronchopneumonia (73) and enteric fever (37). The tuberculosis situation was investigated by Dr C. A. TAYLOR (New Zealand) who concluded that it was not particularly serious.

The infant mortality rate was 106 per 1,000 registered births in 1926, 291.77 in 1936 (the high figure was the result of epidemics of whooping cough and measles) and 64.05 in 1946.

C

Charles Wilecks

# TROPICAL DISEASES BULLETIN

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[No 6

## SUMMARY OF RECENT ABSTRACTS\*

## V LEISHMANIASIS

## VISCERAL LEISHMANIASIS

*Epidemiology. Aetiology. Transmission*

FALCÓN TREJO (p 984) reports kala azar from Badajoz, Spain

An account of leishmaniasis in Greece is given by MALAMOS (p 1), who considers the geographical distribution of kala azar (here a disease of infants), canine leishmaniasis (due to *L. donovani*), and oriental sore. The chief vector of kala azar in Greece is *Phlebotomus major*, and of oriental sore *P. sergenti*, only occasionally is *P. papatasi* involved.

HO *et al* (p 987) have found visceral leishmaniasis in dogs in part of China where kala azar is present. Leishmania were found in the skin of most of the infected dogs.

SHIH LU CHANG (p 1055) describes two media, one semi-solid, the other fluid with a solid base, for cultivation of leishmania and *T. cruzi*. Both give better growth than the media usually employed. For details the original should be consulted. With the solid-base medium, SHI LU CHANG and NEGHERBON (p 1056) have studied the growth characteristics of various species of leishmania, and of *T. cruzi*, but for details the original should be consulted.

PEREIRA and MEDINA (p 188) describe a method of staining leishmania, especially in tissues.

ADLER (p 983) has observed the behaviour of a Sudan strain of *L. donovani* in *P. papatasi*, the infection rate was low in sandflies fed on a diseased hamster. The infection rate provides one means of differentiating strains of *L. donovani*. Differentiation of the various species of *Leishmania* may be determined by consideration of results of cultivation experiments, infection of hamsters and of sandflies. For details the original should be consulted.

DE AZEVEDO and TELHEIRA (p 981) note the various species of *Phlebotomus* found in Lisbon in summer and autumn, and their habitats and blood preferences. Only 2 per cent showed positive precipitin tests with anti-human sera, whereas 22.5 per cent were positive with anti-bovine serum.

DOLMATOVA (p 982) has studied the sandflies of a district in the Caucasus. In this area there are numerous burrows, some occupied by birds, and the

\*The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin* 1947 v 44. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

sandflies breed in these burrows. Several species known elsewhere to transmit kala azar occur here—the author thinks that *P. perniciosus* var. *habe*, is probably a natural vector of *L. donovani* as it can be infected experimentally and attacks man.

SHORTT (p. 511) has answered the criticisms previously made by Malone and Brooks (this Bulletin 194, v. 42, 357) on the experimental work done on the transmission of kala azar by *Phlebotomus argentipes*. FENG and CHENG (p. 1055) report (for the first time) successful transmission of kala azar from dog to hamsters by the bite of *P. chinensis*, and also that hamsters became infected when inoculated with flagellates from *P. argentipes* var. *mongolensis* previously fed on an infected dog.

### Diagnosis Clinical Findings

DR AZEVEDO (p. 834) writing from Portugal, notes that the various standard methods of diagnosis of kala azar may give negative results, and advocates examination of material from the nose for leishmanias. With a platinum loop the mucous membrane is scraped until the surface is broken—in 11 cases examined, 9 were positive. The procedure is simple but it is necessary to break the surface since the organisms are in the histiocytes of the submucosa.

The cephalin-cholesterol flocculation test was found by MAKARI (p. 284) to be strongly positive in eight cases of infantile kala azar.

DHARMENDRA *et al.* (p. 189) have prepared an antigen from Hedrowsky's acid fast bacillus to be used in a complement fixation test for kala azar.

ADLER (p. 983) shows that in leishmanias there is proliferation of the reticulo-endothelial cells and also a secondary round-cell infiltration—he thinks that the latter reaction is a curative one, and that lymphocytes play some part in defence. This reaction is marked in dogs (in which the disease is usually chronic) but is slight in spermophils (in which the disease is acute and fatal).

PARRINELLO (p. 297) reports on the coagulation of the blood in infantile kala azar in Italy.

FELDMAN (p. 297) describes kala azar in a British soldier who had served in the Mediterranean—the disease developed 4 months after return to England. NORMAN (p. 54) mentions a case of long latent period in kala azar.

DEBONO (p. 985) states that in Malta, kala azar is a disease of young children rather than of infants. He describes the incubation period, onset and course of the disease and the means he uses for diagnosis and treatment. It responds well to intra-venous antimony.

### Treatment

VAN DYKE and GILLMORE (p. 512) have tested in hamsters 168 new compounds for activity against the Sudan strain of *L. donovani* but none has proved better than the recognized drug.

The same authors (p. 286) noting that pentavalent antimony compounds are more effective and less toxic than trivalent compounds in leishmaniasis, describe in investigations to find if there is a correlation between therapeutic activity of a drug and the amount of antimony present in liver and spleen of treated animals. The results were essentially negative in that the presence of high concentrations of the drugs (pentavalent compounds) was not synonymous with cure.

KIRK (p. 984) reviews the treatment of kala azar in the Sudan where the use of antimony effects cure in 70 per cent of cases which would almost all be fatal without it. Use of the diamidines has further improved the results of treatment. The appearance of dermal lesions during or after treatment is of good prognostic significance—they may persist 20 years or more without affecting health.

KIRK and SATI (p 885) in the Sudan report favourably on the results achieved in kala azar with sodium antimony gluconate [sodium stibogluconate] given intravenously in concentrated solution, for 6-10 injections, over a short period (as short as 6 days in some cases). The results in a small series were better than when the drug was given in smaller doses over a longer period, and the brevity of the course is in itself an advantage. MAEGRAITH *et al* (p 886) treated eight patients with kala azar (Indian or Mediterranean strains) with sodium stibogluconate, with one death and seven cures. The drug was given intravenously, once or twice daily for 10 days, and severe reactions occurred in five patients, and were attributed to it. In the fatal case there was shock and circulatory failure after the last dose, but the actual cause of this could not be ascertained at post mortem examination. There was no evidence of accumulation or anaphylaxis, nor was it due to a defective batch of the drug. Cure was confirmed parasitologically, sometimes 3-4 months later. CHOUDHURI (p 298) reports cure in 22 of 23 patients with kala azar (in India) treated with sodium antimony gluconate (Stibatin).

SARROUY *et al* (p 55) have used a new antimony preparation (antimoniate of N-methylglucamine) in the treatment of a child with kala azar, it was successful, but the dosage has not yet been determined, though the preparation is said to be only half as toxic as Pentastib. DURAND *et al* (p 56) report further use of this drug, confirming its value and low toxicity. It is rapidly excreted by the kidneys. They treated 6 cases with very good results, though sufficient time has not yet elapsed to decide if permanent cure has been obtained. SARROUY *et al* (p 807) report three more cases successfully treated with this drug, which they regard as the most efficacious yet discovered.

The antimony content of different batches of urea stibamine varies, and the drug is not a compound of uniform formula. BOSE *et al* (p 189) have worked out the toxic dose for mice, but there is considerable variation. Assay of the drug must still be made biologically, since the relation of antimony content to toxicity is not known, and there is no indication which fraction is therapeutically active. To avoid the toxic symptoms which often arise as a result of treatment with urea stibamine, Ho (p 189) in China gives relatively small doses for kala azar, and has found that with these, given once or twice each week, most cases are cured.

HARRISON and FULTON (p 190) describe the changes which take place in the spleen of *Cricetus auratus* on infection with *L. donovani*, and show that although the enlarged spleen diminishes in size on treatment with 2-hydroxy stilbamidine, there is always a residual splenomegaly, even after cure. FULTON and DUNITZ (p 988) discuss the constitution of the toxic substance created when stilbamidine is irradiated. SALTZMAN (p 988) describes a method for estimation of stilbamidine in urine and blood, but FULTON, in comment, criticizes the technique employed.

ADLER and TCHERNOMORETZ (p 406) have failed to cure dogs, naturally infected with *L. infantum*, with stilbamidine or neostibosan. There is always a residual skin and gland infection, even after intensive treatment, and the authors therefore advise that as such dogs serve as a reservoir for disease in man they should be removed from endemic centres or destroyed.

#### CUTANEOUS AND MUCO-CUTANEOUS LEISHMANIASIS

STEINHAEUER (p 987) describes the recurrent form of cutaneous leishmaniasis which is common in Palestine. This form simulates lupus vulgaris, and leishmania are difficult to demonstrate except by cultural methods. The intradermal leishmania vaccine reaction is positive in 97 per cent of cases, and biopsy shows characteristic tuberculoid structure. He reports a case of a

verrucose form of this disease which though common in South America, is rare in the Middle East.

PIERS (p. 889) reports a case of muco-cutaneous leishmaniasis from central Kenya, and notes a few cases of kala-azar from the same area. This is the first time that cases have been reported from this place and it is not known whether a focus existed before or whether the disease has been introduced as a result of troop movements from Abyssinia. Penicillin treatment produced some improvement in the muco-cutaneous lesions.

AXSAKI (p. 191) uses penicillin to control bacterial infection when isolating *L. tropica* in culture. He adds 1,250 units to each cubic centimetre of N.C.N. medium.

AXSAKI (p. 587) describes a substance in commercial preparations of Iramin B which stimulates growth of *L. tropica* in culture, and another which inhibits it. The former is heat labile, the latter heat-stable.

JERACE (p. 808) has found *P. perforans* in the Abruzzi area of Italy, where it is the vector of oriental sore.

Working in Calabria, TIMPANO (p. 280) claims to have transmitted oriental sore from man to man, three times by mosquitoes and once by sandflies. The insects (and houseflies) were allowed to feed on sores, and were then transferred to healthy persons, on whom they fed. He also claims to have found flagellates in the pharynx and stomach of two mosquitoes and a sandfly. In comment, WEXROX remarks that the arrangement of the experiments seemed to favour mechanical transmission rather than development of leishmania in the flies, and comments on the shortness of the incubation period (17-15 days).

DOLMATOVA (p. 587) has made observations on the biology of *P. papatasi*, *P. sergenti* and other sandflies in a focus of oriental sore in Tadzhikistan. They have, apparently, no food preferences, but feed on the most accessible animals.

KIRYAN (p. 190) states that *P. rousselli* is probably the common transmitter of cutaneous leishmaniasis in the French Sudan.

The histo-pathological processes involved in the invasion of the tissues of man by *L. tropica* have been described by LIVINGSON and SKABOVSKAYA (p. 888), and details should be sought in the original abstract. The infection was initiated by inoculation of *L. tropica* from the moist type of human oriental sore.

DOSTROVSKY and SAGHER (p. 1058) have found in a number of trials, that the culture method of diagnosis in oriental sore gives more positive results than examination of smears for leishmaniasis, particularly in old, chronic cases, in which the lesions may resemble those of lupus or syphilis. SAGHER (p. 899) has used a vaccine of *L. tropica*, in graded dilutions, for skin tests in cases of oriental sore of various types. He concludes that in the recurrent type (with infection lasting more than one year) there is a more pronounced allergic component than in the nodular form (with infection of less than one year). DOSTROVSKY and SAGHER (p. 887) have found the intracutaneous test (with the vaccine prepared by the former) positive in most cases of oriental sore (either nodular or recurrent) tested in the Jerusalem area, whereas examination of the lesions for parasites was negative in more than half of the cases. The chances of non-specific reactions are small.

ROMANA *et al.* (p. 310) have found a focus of cutaneous leishmaniasis in Tucumán, Argentina.

PISSODI and BARRETO (p. 300) summarize the evidence that American cutaneous leishmaniasis is most common in men whose work takes them into forests where sandflies abound.

Charles Ifeoluwa

## RABIES

UNGARI, C    Meningoencefalomielite da virus rabico a decorso clinico anomalo  
[Meningo-encephalitis due to Rabies Virus, having an Atypical Clinical  
Course] *Pediatrics* 1943, Feb, v 51, No 2, 52-8

The author refers to the difficulties experienced in deciding, when an acute ascending paralysis of the Landry type occurs at the end of or shortly after completion of anti-rabies treatment, whether it is a latent encephalomyelitis activated during the treatment, a paralytic accident of vaccine treatment or a case of rabies caused by street virus or fixed virus modified by vaccination

A case of street virus infection which followed an atypical course is described

A girl aged 7 years was bitten on the face by a stray dog, later confirmed by biological tests as having been rabid. Local disinfection was effected and anti-tetanus serum given within a few minutes, intensive anti-rabies treatment was commenced with PUNTOVI's phenolized vaccine within 48 hours. On the 21st day of treatment (23 days from the date of bite), the child suddenly developed high fever, followed two days later by signs of a paralysis which ascended from the lower limbs to the cranial nerves before death supervened on the 9th day of illness.

The main symptoms were those of paralysis with fairly well marked meningeal signs, itching in the bite scar and changes in the mental state (agitation, hallucinations, delirium). At no time was there hydrophobia or aerophobia, deglutition remaining comparatively unimpaired until death.

Histological examination of the brain revealed no Negri bodies, but the so-called Babes nodules were found in the superior olivary body.

Biological tests made on two guinea-pigs by the inoculation of bulbar material resulted in the death of the animals on the 18th day, with the presence of numerous and typical Negri bodies in the horn of Ammon. A second and third passage resulted in death of the test guinea-pigs on the 11th and on the 7th days respectively, with similar post mortem recovery of Negri bodies. The diagnosis of street virus was therefore established.

The difficulties of establishing a differential diagnosis on clinical grounds alone are discussed

G Stuart

CAMPBELL, T C & DEFRIES, R D    Some Observations on the Preparation of  
Rabies Vaccine using Phenol [Abstract.] *Canadian J Pub Health*  
1948, Feb, v 39 No 2, 82

The introduction of the mouse test by Webster in 1939 made possible the determination of the antigenicity of rabies vaccines. As a result vaccines of greater antigenic value have been prepared. A modification of the method of preparing rabies vaccine employing phenol (Semple method) is described in which phenol, 1 per cent, is added to a 30 per cent suspension of rabid brain tissue in place of an 8 per cent suspension as usually employed in the preparation of rabies vaccine by the Semple method. The antigenic value of the vaccines so prepared has exceeded the minimum standard as recently established by the National Institute of Health, Washington, namely protection against 1000 MLD of challenge virus. A change, also, in the strain of virus in the preparation of both human and veterinary vaccines may be a contributing factor to their improved antigenicity. Vaccines for veterinary use prepared from rabid calf brain tissue possess a much greater antigenic value than vaccines made from rabbit brain tissue. Observations over a period of years of veterinary vaccines prepared from calf brain and processed by this method indicate that their potency is retained for a much longer period than that of

vaccines prepared by the standard Semple method for human use. The destructive action of freezing on rabies vaccines containing phenol is low. Further supporting evidence of this fact is supplied.

HABEL, R. & WRIGHT, J. T. Some Factors Influencing the Mouse Potency Test for Rabies Vaccine. *Pub. Health Rep. Wash.* 1948 Jan. 9 v. 63, No. 7 44-55 3 figs

A mouse test for the potency titration of rabies vaccine was first described by HABEL in 1940 since when official recognition has ensured its routine adoption as the basis of a minimal potency requirement of all rabies vaccines produced in the U.S.A. for human or veterinary use.

Variations in the results of the test have however been observed by workers in different laboratories and it was in order to determine the factors responsible for such variations and, if possible to eliminate them that the study described in this paper was undertaken.

In this connexion the influence of (a) technician, (b) strain of mice and (c) strain of test virus was closely investigated, with the result that in (b) and in (c) a probable explanation was found.

Thus as regards (b) it emerged that with the technique employed in the standard test strains of mice at the age of 4 weeks may vary in their ability to be immunized with a particular rabies virus. As regards (c) it was shown that a wide variation of invasiveness (i.e. the ability to cause rabies in immunized mice) exists among fixed viruses even if as in the present study substrains of the original Paris (Pasteur) fixed virus are used. The substrains in question had been carried in different laboratories over a period of years by different individuals using different intracerebral passage techniques; any differences in their present characteristics must therefore have occurred through repeated animal passages over a long period of time.

In the light of the above findings, the authors consider it necessary to standardize the technique of the test and in this sense detail requirements for an acceptable determination of potency.

Of these requirements reference need only be made here to (a) type of test mouse and (b) the standard test virus.

(a) Type of test mouse.—The test is based on the use of white Swiss mice of either sex approximately four weeks old uniform in weight (11-13 gm.).

(b) The standard test virus.—A standard test virus will be supplied by the National Institute of Health preferably only on request at approximately yearly intervals. The use of such a standard virus will largely eliminate virus variations from routine potency testing. A standard virus may be obtained from pooled frozen virus which, as has been shown, will retain its titre for at least 10 months with relatively slight variation in the titration end points from test to test. Further to reduce the possibility of a standard virus changing its characteristics because of animal passage in different laboratories, the number of passages of the reference standard test virus actually used in determinations of potency should be held to a minimum. C. Stuart

AMERICAN J. PUB. HEALTH. 1948, Jan. v. 38, No. 1 Pt. 1 97-9 Recommended Methods for Rabies Control. Adopted by the Committee on Research and Standards, October 6 1947 American Public Health Association

A Conference on Rabies held in April 1947 at the University of Pennsylvania reached complete agreement on the means whereby rabies control, undertaken on a national basis, could best be effected in the U.S.A.



The following paragraphs summarize the principal recommendations

1 Active cooperation on the part of the Federal Government

(a) by contributing funds and personnel to affected States ,

(b) by establishing a central bureau for the collection from and distribution to States, agencies and individuals concerned in the control programme, all information on the incidence among animal species and on the place of occurrence of rabies

2 Prime consideration should be given to (a) adequate diagnostic facilities, (b) the control of animals capable of transmitting the disease , and (c) mass immunization of susceptible animals, particularly dogs

(a) and (b) need no comment , they conform to orthodox procedure

As regards (c) it is held that the vaccination of dogs, combined with other control measures, provides the most satisfactory method for the prompt control of rabies. Evidence shows that a single 5 ml subcutaneous injection of an accepted canine rabies vaccine is effective in a mass vaccination campaign, but that the administration of three doses of such vaccine in 5 ml amounts, one week apart, affords greater immunization. To secure permanent reduction in the number of susceptible dogs, annual immunization is advocated.

Vaccinated dogs, identifiable as such by suitable tags, may be allowed at large 30 days after vaccination. Finally, the need is emphasized for a comprehensive educational programme to bring the subject of rabies and its control before the public

G. Stuart

KORNS, R. F. & ZEISSIG, A. Dog, Fox, and Cattle Rabies in New York State Evaluation of Vaccination in Dogs *Amer J Pub Health* 1948, Jan v 38, No 1, Pt 1, 50-65, 11 figs

This article describes an epizootic of rabies continuing since 1943 in New York State and details measures for its control among the animal species affected there

1 *Incidence*—The epizootic has been characterized by the introduction and spread of the virus among foxes and cattle, with a concurrent sharp decline in canine rabies—a decrease ascribed in large measure to the extensive practice of dog vaccination. Thus in 1946, rabies was reported in 377 dogs, 308 foxes and 440 cows, during the first nine months of 1947, it was reported in only 40 dogs, but in 218 foxes and 173 cows. Rabies in cattle seems clearly to have been due to the bites of rabid foxes, fox rabies, with, as corollary, cattle rabies, has spread in a slow radial fashion over a period of two years.

2 *Control Measures*—(a) Control of the dog problem—Following on the acceptance of the HABEL rabies vaccine potency test and on the demonstrated value of approved anti-rabies vaccines in canine prophylaxis, a further measure of control has been added to that previously in force, *viz* restriction of the activity of dogs in areas where rabies was certified by the State Commissioner of Health to be present.

To be effective, mass vaccination of dogs presupposes immunization, spread over an area at least county-wide, of not less than 70 per cent of the enumerated dog population, it should be carried out in as short a period as possible, preferably within a month, so that the majority of the dogs in the area will attain maximum levels of immunity about the same time. When this percentage is achieved, the Commissioner of Health may designate 'certified areas' (*i.e.*, where rabies exists) as areas in which vaccinated dogs may be allowed to run at large—such designation to terminate in 12 months unless the immune status of the dog population is maintained by revaccination. The general practice has been to give each dog only one injection of 5 ml of vaccine, repeated yearly.

Evidence of the value of mass vaccination is adduced from the experience of 10 counties wherein 8 per cent. of the enumerated dogs were immunized; there the rabies attack rate in non-vaccinated dogs was 15.8 times as great as that in vaccinated dogs observed during the same period and in the same area.

(b) General recommendations for rabies control include: mass vaccination, combined with ordinary measures of dog control; anti-rabies measures to be initiated as soon as incidence is reported in adjacent counties; the appointment of a full-time veterinary consultant on State level, to promote and supervise the control programme; the contribution of financial aid to counties for dog vaccination clinics; adequate education of the public concerning rabies.

(c) Control of the fox problem.—This has been attempted by the creation, through trapping, of a zone of fox scarcity surrounding the infected area.

G. Stuart

## MALARIA

SAUTAREK, J. Malaria in Czechoslovakia after World War II. *J. Parasitology* 1947 Dec. 33 No. 4, 563-8.

Although natural conditions favourable to the propagation of malaria exist in Czechoslovakia, malaria was unknown in the western parts of that country since the 1850's until the end of World War II. Then, two exodus of troops and civil populations and changing epidemiological conditions caused the occurrence of malaria in two territories which are quite apart from each other, namely Southern Moravia and north-western Bohemia.

The anophelines of Czechoslovakia are found in the plains and in the lower hilly country; rarely are they found in free nature but are mostly met with in warm quiet stables and occasionally in human dwellings. The species found are *A. chloris*, *A. maculipennis maculipennis* and *A. m. messeae*.

The part of Southern Moravia which was affected is flat and richly irrigated agricultural country. Wartime destruction of stables and cattle on a large scale caused the mosquitoes to lose their predominantly zoophilic character and to turn to human hosts. The retreating German armies withdrawing through Moravia were followed by the Russian army which contained Romanian units from the highly endemic Balkans; soldiers carrying malaria parasites passed the infection on to mosquitoes and hence to the human population. Furthermore, damaged sewage and irrigation systems and bomb craters became breeding places for mosquitoes.

The affected area in north-west Bohemia was infected from a different source. This territory is a lignitic coal-mining district with many shallow shafts; in deserted and sunken mines there are undisturbed pools which breed large numbers of mosquitoes. During the war, large synthetic petrol factory was built and labourers, including prisoners of war were brought from many countries, such as the Balkans and Italy; with them, among them, are numerous persons with untreated malaria.

The author is unable to provide detailed statistics, as the official reports did not distinguish fresh cases of domestic origin from malaria contracted outside Czechoslovakia. He draws, however, on cases reported in the local medical journals and refers to 14 cases in Moravia and in Bohemia in the first year after the war and 31 and 10 respectively in 1946. The increase in 1946 is explained by lack of and incomplete cure and it is added that the form of malaria seen in Czechoslovakia shows great tendency to relapse.

## Malaria

Vol 45, No 6]

All infections were caused by *P vivax* and infections with two generations, showing a quotidian fever, were common. An outstanding feature of the infection as seen in Czechoslovakia is the severe initial anaemia, characterized by red cell counts as low as 2 million per cmm and haemoglobin often lower than 50 per cent. Such a severe anaemia is not found in the established endemic areas of Europe, and the relatively malignant course of *P vivax* infections in Czechoslovakia is explained by lack of previous infection and a generally lowered resistance. The disease was successfully treated with the usual doses of quinine and mepacrine.

It is remarkable that no great epidemics occurred, in spite of the conditions favourable to them, it is suggested that energetic isolation and treatment helped to localize the disease.

The present importation of further labourers from the Balkans and Italy may cause a fresh wave of malaria, and this possibility must be taken into account by the health authorities for some years to come.

[This is yet another example of the disruptive effects of man-made destruction of biological equilibrium even when such interference is benevolent—as in the case of large-scale, aerial DDT spraying and its effects on wild life, or the mutations brought about by bacterial resistance to newer chemotherapeutic agents—some of the ultimate biological implications are often unpredictable.]

H J O'D Burke-Gaffney

'ETA, T. L'infezione malarica a Gondar [Malarial Infection in Gondar] *Riv di Malariaologia* 1947, Dec, v 26, No 6, 296-9

The English summary appended to the paper is as follows —

"After stating that an estimate of the malarial conditions in a certain area must be based on the human factor, surroundings and seasonal and anopheline factors, the author briefly discusses these subjects, dwelling particularly on the anopheline factor.

"From larvae breeding and the capture of culicine adults in the Gondar zone (Ethiopia), the author had following results: several specimens of *Diptera* (gen *Culex*) and only two *Anopheles* *A cinereus* and *A demeilloni*. None of these are known to be malaria vectors. The author therefore thinks that malaria control in Gondar is unnecessary."

CIUCA M, BALIFF, L & CHELARESCO, M. Formes dégénérées de sporozoïtes dans l'infection expérimentale d *A maculipennis* v *atroparvus*, *P vivax* et à *P falciparum* [Abnormal Forms of Sporozoites in Experimental Infection of *A maculipennis atroparvus* with *P vivax* and *P falciparum*] *Liber Jubilans J Rodham* (Soc Belge Méd Trop, Brussels) 1947, Dec, 131-46 2 figs

During the last 15 years work on experimental malaria has been carried out at the Socola station in Rumania. The authors used a Madagascar strain of *P vivax* and a local strain of *P falciparum*. Transmission to cases of G P I was effected by blood inoculation and by sporozoites from *Anopheles maculipennis* var *atroparvus*. The sporozoite infections resulted from (a) mosquito bites, (b) bites plus intravenous inoculations of glands, and (c) intravenous inoculations of glands alone. The second method was slightly more successful but about 90 per cent of all the patients developed the disease.

Fifty per cent of 774 *Anopheles*, fed on *P vivax* carriers, became infective. 17.7 per cent of these infections exhibited abnormal sporozoites.

Fifty-five per cent of 688 *Anopheles*, fed on *P falciparum* carriers, became infective. 32.4 per cent of these infections exhibited abnormal sporozoites.

These modifications in the appearance of the sporozoite were primarily a thickening of its body and the conversion of its chromatin into a blurred mass lying in a colourless vacuole. The shape undergoes various contortions. The abnormalities bore no apparent relation to temperature or humidity variations, nor to season.

[Examination of the protocols reveals that abnormal forms were commoner among the sporozoites which first reached the glands, and that in the older mosquitoes, degeneration was less likely to occur] P. C. C. GARHAM

SHORTT H. L., GARHAM P. C. C., CUSTELL, C. & SMITH P. C. The Pre-erythrocytic Stage of Human Malaria, *Parasitology* 1948, Mar 20 547

The observations on *Plasmodium cynomolgi* by SHORTT & GARHAM of the pre-erythrocytic stage of development in the liver of the monkey led them to suspect that *Plasmodium vivax* would be found to have a similar cycle in the liver [this *Bulletin* 1948, v 45 368]. Accordingly a large number of *Anopheles maculipennis atroparvus* infected with *P. vivax* were fed on a patient at the Horton Hospital for Mental Diseases on two successive days. In addition an emulsion of infected salivary glands was injected intravenously. Seven days after the first feeding of the mosquitoes a biopsy was performed under local analgesia and a portion of liver removed for examination. In it were found plasmodial masses studded with chromatin particles very similar to those previously found in the monkey infected with *P. cynomolgi*. The masses measured up to  $4\mu$  in diameter and in some cases had the vacuoles noted in *P. cynomolgi*. There seems to be no doubt that the bodies are the pre-erythrocytic stages of development of *P. vivax* in man. The material is being studied and a further report is promised. C. M. HEWITT

HUFF C. G. Periodos exoeritrocitarios de los parásitos de la malaria. (Erythrocytic Stages of Malaria Parasites.) *Medicina, Mexico* 1948, Jan. 25 28. No. 548, 23-33.

A review

BRADLEY L. C. Note sullo sviluppo dell' *Anopheles sacharovi* sulla costa del Veneto [The Development of *Anopheles sacharovi* on the Venetian Coast. *Rivista di Parasiti* Rome 1947 Dec. 8, No. 4 197-202. (19 refs. English summary (8 lines)]

The highly malarious area in the north-east of Italy is limited to a coastal strip some 10 to 15 km. in width from Ravenna to Trieste. This corresponds to the area of distribution of the chief vector *A. sacharovi*. It is generally assumed that this species has a marked partiality for saline water in which to lay its eggs and that the presence of saline marshes and lagoons in this area explains the high incidence of malaria. The author's observations do not confirm this supposition. He found *A. sacharovi* breeding in water with a very low saline content. Norma White

THOMSON R. C. Mourhead. Studies on *Anopheles gambiae* and *A. melis* in and around Lagos. *Bull. Entomol. Res.* 1948 Feb. v 38, Pl. 4 527-58. 1 map 3 text figs. & 5 figs. on 1 pl. 125 refs.

The presence of an additional dark band on the palps of about one-third of female adult *Anopheles melis* in the Freetown area enables an estimate of *melis* population possible without recourse to the laborious method of

distinction to distinguish *gambiae* from *melas*. This does not apply in the Lagos area, as the number of 4-banded *melas* is too small, of 1,200 egg batches examined, 99.7 per cent were readily distinguishable into *gambiae* or *melas*.

The seasonal incidence of *melas* and *gambiae* in houses is tabulated for villages, on the coastal strip of the mainland to the north and west of Lagos Island for Lagos Town and for creek villages to the east. In the first group numbers are about equal on the coastal fringe, but *melas* fades out at a short distance (1 mile) from the coast, in Lagos town, on an island, *gambiae* is predominant, in the third group to the east, which is associated with mangrove swamp, *melas* is the most abundant. Despite these generalizations, catching stations within a short distance of each other may have widely different mosquito populations. The abundance of *melas* is mainly determined by tidal movements which are variable and unpredictable when compared to the Freetown estuary. In contrast, the abundance of *gambiae* is related to the rainfall, a great reduction in numbers occurring in the dry season, November to March. Finally, in any one village the seasonal incidence of both mosquitoes may follow entirely different courses in consecutive years.

The sporozoite rate of *gambiae* (10 per cent) is consistently higher than that of *melas* (3.5 per cent). Peak production of *gambiae* is associated with a lowered sporozoite rate, but in the last three months of the year when the *gambiae* population is low, the rate is higher and may reach 29 per cent. The sporozoite rate of *melas* tends to conform to the numbers of females present in houses and is comparable to the Freetown Estuary rate of 4.2 per cent. [See TREDRE, this *Bulletin*, 1947, v 44, 488]. Observations on resting places, both indoor and outdoor, indicate that *gambiae* in the gravid state made use of the house to a much greater extent than did gravid *melas*, in one village it was estimated that through the favourable six months of the year, *melas* made use of outside resting places to 10 times the extent that *gambiae* did. The degree to which *gambiae* or *melas* favour outside resting places is of considerable importance in relation to the use of residual insecticide in houses as a control measure.

The movement of mosquitoes in and out of houses was investigated by the use of experimental huts fitted with a special window trap, this method resulted from the observation that exterior waning light is a powerful attraction to mosquitoes indoors. It was noted that 90 per cent of blood feeding by *melas* and *gambiae* took place after midnight, the period of greatest activity being between 4 a.m. and dawn, 43 per cent of *melas* and 26 per cent of *gambiae* which had entered and fed left by dawn the same night. In the case of *melas* which remained in the hut, all gravid and 70 per cent of half-gravid females left at dusk.

The author was successful in getting swarming, mating and fertilization of *melas* and *gambiae* to take place in 1 ft.-cube cages. Data of cross-fertilization experiments are quoted, hybrid males were sterile.

The breeding areas of *melas* are very difficult to localize and the whole tidal swamp area covered with *Paspalum* is suspect, the comprehensive nature of the tidal swamp reclamation should eliminate all potential breeding places [GILROY and CHWATT, this *Bulletin*, 1945, v 42, 786]. Breeding areas of *A. gambiae* are the typical open shallow water collections, which include almost dry wells, rain pools and puddles and sedge swamps. The last-named may be just below high water mark and prolific breeding will cease abruptly if a fortuitous tide floods the area. In Lagos Town, the steady progress in street drainage and swamp filling has practically eliminated breeding places. However, the author draws attention to the instance of a single small garden-compound producing in the rainy season a *gambiae* output sufficiently enormous to affect a whole corner of the city and nullify good work in process elsewhere.

(There is no reference to the possibility of the invasion of Lagos Town by malarial mosquitoes from across the surrounding waters and the evidence of this paper suggests that after the extensive swamp reclamation measures in the district, the town and port may be kept relatively free of malaria vectors by a vigilant sanitary staff.)

R. Ford Trill

SCHWETZ, J. Sur le lac Tumba. Notes géographiques, entomologiques et médicales. (Moustiques et paludisme tschadiens et trypanosomiase.) Lake Tumba. Geographical, Entomological and Medical Notes: Mosquitoes and Malaria. Tsetse Flies and Trypanosomiasis. Inst. Roy. Colonial B. et. Bull. des Sciences 1917 v. 18, No 2, 482-511 1 map & 3 figs. on pl.

Lake Tumba lies near the l ft bank of the River Congo about 100 kilometres south of the Equator. A winding channel about 15 km. long unites the waters of lake and river. Such little current as is manifest in this channel is towards the lake in the rainy season and towards the river when the water is low. The lake is about 43 km. long (north-south) and about 22 km. broad. Its shores are indented by very numerous bays and capes. Several rivers discharge into the lake the two largest being the Lola into the south of the lake, and the Ngombe into the north-east.

The author spent three weeks investigating conditions on the shores of Lake Tumba, making his headquarters at Bikoro about the middle of the eastern shore. A motoring road, 128 km., joins Bikoro to Coquilhatville which lies on the Equator almost due north of the lake.

The banks of the lake are for the most part high and gently sloping wooded and without grassy or marshy edge favourable to mosquito breeding. In such places mosquitoes are almost non-existent. But on certain small bays, near villages swampy conditions near the mouths of small streams are productive of mosquitoes: these are still more numerous near the mouths and along the banks of the larger rivers.

*A. gambiae* and *A. funestus* were the most prevalent *Anopheles* along the shores of Lake Tumba. These two species are in general rather rare in this part of the Congo and neither has been incriminated as a vector of malaria. *A. marshii* var. *marshii* the predominant anopheline at Coquilhatville was rare as was *A. gambiae*. *Aedes aegypti* was not found. *Mansonioides* were very rare.

*G. sima palpalis* was rare along the shores of the lake but very prevalent along the banks of the rivers that flow into it. Several specimens of *G. fuscicornis* were also captured.

*Simulium albi-irradiatum* was very prevalent along the shores of the lake they lay during daytime but were most active towards evening. Phlebotomids were also plentiful. *Ph. africanus*, *Ph. africanus*, *Ph. desertorum* and *Ph. schultzei*.

The blood of 448 inhabitants of four lakeside villages was examined. This showed malaria to be endemic. Parasite rates were high but the number of parasites was low. *P. falciparum* was by far the most prevalent species. *P. vivax* was only found in two films. *Acantaxanthromus periti* was frequently encountered. *Loa loa* occasionally.

The author found a considerable number of villagers who were undergoing treatment for sleeping sickness or who had been treated but little or no evidence that they were or had been infected. The diagnoses had been made on altogether insufficient evidence. In only one of the 448 individuals examined, thick drop and smears were trypanosomes discovered. He was a schoolboy in the Catholic Mission School at Bikoro. Sleeping sickness exists in this region but cases are extremely rare.

Norman White

MILLER, A., BURGESS, R. W. & CARPENTER, S. J. Potentialities of Transportation of Exotic Anophelines by Airplane. *J. National Malaria Soc.* 1947, Dec., v 6, No 4, 227-43 [27 refs.]

The number of aeroplanes entering the United States of America each year is estimated to be 35,000, or nearly 100 per day. This volume of air traffic is increasing and the time spent on journeys is being reduced, so that very soon no place will be more than two days' flight from the U.S.A. The bulk of the traffic at present comes from Latin America and it might be expected that the greatest danger of importing mosquitoes lies in that quarter, but from the climatic point of view, Europe and the non-tropical areas correspond more closely with conditions in the U.S.A. as a whole, and it may be more likely that species transported from such places would be more easily established.

The authors review the history of the development of international air traffic and discuss the practical application of the "International Sanitary Convention for Aerial Navigation". Figures are quoted from reports showing, for example, that in the year July 1st, 1944 to June 30th, 1945, 1,418 mosquitoes (158 alive) were among 24,930 insects found on 12,367 aircraft. There were 1,339 culicines (142 alive) of 21 species and 79 anophelines (16 alive) of 9 species. The identified anophelines were *Anopheles albimanus*, 10 alive out of 34 found, *A. pseudopunctipennis*, 2 alive out of 4, *A. quadrimaculatus*, 3 alive out of 5, *A. punctipennis*, 1 living, *A. crucians*, 19 dead, and 1 dead specimen of each of the following, *A. grabhami*, *A. maculipennis aztecus* (?), *A. neomaculipalpus*, and 4 *pharoensis*. The last-named and one Indian culicine are the only Old World species in the reports that are not already present in the U.S.A.

It is thought that not more than 10 per cent of mosquitoes are detected in the planes, and the authors speculate on the hypothetical number of exotic mosquitoes likely to be imported in one year and arrive at the following figures for 100 aircraft: 115 mosquitoes (13 alive), 64 anophelines (13 alive), and 1 exotic species including 0.3 to 0.6 exotic anophelines. At this calculation 35,000 aircraft would bring in 350 exotic mosquitoes of which 100 to 200 might be anophelines not already recorded in the States or 10 to 25 living anophelines per year, but during the last three years, no viable anopheline has been detected in the incoming aircraft, owing to the efficiency of the preventive measures. Nevertheless, in spite of the small chances of importation of these mosquitoes, prudence and experience demand a continuance and extension of mosquito control around airports, and the disinsectization of the aircraft. The efficiency of insecticides is improving, as also are the methods of application, and the likelihood of new malaria vectors becoming established in the United States remains, in the opinion of the authors, a potential problem but not an acute one.

H. S. Leeson

GIGLIOLI, G. An Investigation of the House-frequenting Habits of Mosquitoes of the British Guiana Coastland in relation to the Use of DDT. *Amer. J. Trop. Med.* 1948, Jan., v 28, No 1, 43-70, 6 figs. & 1 graph.

In the first quarter of 1945, SYMES and HADAWAY [this *Bulletin*, 1945, v 42, 785] initiated in British Guiana the spraying of houses with DDT. Progressive expansion of this work necessitated preliminary mosquito surveys of which this paper is descriptive. These were confined to the coastal zone, the topography and meteorology being briefly referred to. The precise localities selected for description can be taken as prototypes of ecological conditions prevailing in urban, suburban, village and rural areas of the coastland of British Guiana. [Several excellent photographs are included.] Monthly morning mosquito captures in houses are tabulated for each locality for periods varying from two

to fifteen months. In one locality an experimental hut enabled 7-hourly catches to be recorded. A Shannon down trap with animal bait was used in this area primarily to estimate the *A. gambiae*'s population, but a table of all captures is given.

The mosquito species encountered were nine in number of which *A. gambiae*, *A. albopictus* and *C. univittatus* (species not determined) were rare. *Aedes triseriatus* and *Aedes canadensis* rarely frequent houses. *Aedes aegypti* is subject to control measures. *Culex fatigans* and *Anopheles* sp. accounted for 86 and 23 per cent. respectively of all captures. *Anopheles* varied in different localities. A description is given of the habits, breeding places, etc. of each of the above mosquitoes.

The average *A. darlingi* (the malaria vector) catch per room is as follows —

Locality	Surroundings	Mosquito Catch per room
Lesignan (East coast)	Irrigated cane lands	34.7
Triumph village (East coast)	Irrigated cane lands, inland rice fields and provision gardens	46.3
Mina Repos pasture (East coast)	Open ventilated front land pastures and rice fields	0.96
Lodge village	Georgetown suburb	1.05
Worthingtonville	Georgetown city ward	0.23
La Grange (West bank, Demetara)	Irrigated inland rice fields and provision gardens	22

The author concludes that the highly domestic biting and resting habits of *A. darlingi* and *Aedes aegypti* render the prospects of control by DDT house-spraying (as a residual insecticide) excellent.

*Culex fatigans* is variable in its biting and resting habits and it is expected that this control method will have little effect on the total incidence.

R. Ford T. Cole

LEONARDI G. Citomorfologia e dinamica midollare nelle prime fasi della malaria indotta. (The Bone Marrow in the Early Stages of Induced Malaria. *Riv. di Malariologia* 1947 Dec. v. 23 No. 8 287-82.)

The English summary appended to the paper is as follows —

The author studied the behaviour of the haemopoietic marrow in 8 progressive paralytic patients inoculated with *Anopheles* (3 *P. tritaen* and 5 *P. f. parvus*). The sternal punctures were carried out in series, beginning before the inoculation and continuing until the onset of the disease.

The author having thus established the starting ground (anatomical functioning of the marrow in the progressive paralytic patients) studied the results following inoculation and observed that during the incubation period and the very first phases of the disease the marrow assumes a prevalently erythroblastic orientation, without a constant and prevailing reaction of the reticulum-endothelium.

HECHBERG J. & BERNHARD D. Studies on Liver Damage in Acute Malaria. *Trans. Roy. Soc. Trop. Med. & Hyg.* 1948 Jan. 41 No. 4 533-44 graphs. (23 refs.)

The authors have investigated the Weltmann reaction in 96 cases of naturally acquired *P. f.* and *P. f. parvus* malaria. This reaction measures the



coagulability of the patient's serum in solutions of calcium chloride, this is apparently governed in some way by the globulin content. Sixty-six cases showed increased coagulability. Of these, a high percentage showed changes in cephalin-cholesterol and cholesterol ester fractions of the serum, but there was no correlation between the degree of this reduction and value of the Weltmann reaction, red cell count or sensitivity of the erythrocytes to lysis in bile solution [MER *et al* this *Bulletin*, 1941, v 38, 562]. On the other hand, there was a close relation between changes in the Weltmann reaction (a shift to the right, i.e., coagulation of serum in lower calcium chloride concentrations than normal) and the sensitivity of the erythrocytes to lysis in bile solution.

According to the authors, the results of the Weltmann reaction and the Chorine test (both of which are dependent on certain serum globulins) indicate hepatic damage, since the globulins are synthesized in the liver. Kleeberg claims that "since in all acute haemolytic anaemias the W R (*sic*) quickly shifts markedly to the right, a sudden shift" (to the right in the Weltmann reaction) "in malaria is probably indicative of imminent blackwater fever."

[It would be more profitable at this stage to investigate quantitatively the changes in plasma proteins which actually occur in malaria (as for example was attempted by DOLE and EMERSON, this *Bulletin*, 1946, v 43, 624) than to multiply tests which appear basically non-specific.]

The authors' habit of referring to the Weltmann reaction as the "W R" is both irritating and confusing.] B G Macgrath

RADVAN, I & APREOTESCI, C. La bilirubinémie paludéenne par rapport à la physiopathologie et à la thérapeutique [Malarial Bilirubinaemia in relation to Pathology and Treatment] *Riv di Malariaologia* 1947, Aug., v 26 No 4 183-90

BYLMEYER, J & WINCKEL, C W F. Induced Malaria for Treatment of General Paralysis. *J Trop Med & Hyg* 1948, Feb., v 51, No 2, 27-33, 2 charts

A centre for the provision of malaria parasites for the treatment of general paralysis of the insane in Holland was started in 1921. This article, by two malarialogists who have studied malaria in the field and at the Psychiatric Clinic in Amsterdam, deals with some of the many problems encountered in connexion with induced malaria as employed for therapy purposes. The two species of malaria parasite used are *P vivax* and *P malariae*. *P vivax* is preferable to *P malariae* because it produces the necessary number of chills and is readily controlled by anti-malarial drugs.

It is pointed out that infection is readily produced by infected blood and by infected mosquitoes. One advantage of inducing fever by blood inoculation is that the patients never relapse, but, on the other hand, there is some risk of bacterial contamination by this method, especially when some time elapses between taking parasitic blood from a donor and injecting it into the recipient.

For some time the local indigenous strain was used, but this was not very satisfactory. It was found that with the local strain the incubation period was frequently of long duration, six to nine months. The Horton (Madagascar) strain is now used and is proving more satisfactory. Patients who are found to be immune to *P vivax* are infected with *P malariae* and fever develops satisfactorily as there is no cross immunity between the species. *P falciparum* is not used, as it is considered to be too dangerous. The authors state that the number of patients admitted to their clinic is too few to warrant the employment of three different strains of parasite, [Presumably they mean *species* and not *strains*].

Although *P. malariae* has been employed at their clinic for many years, on only one occasion have they succeeded in infecting the local vector (*An. funicularis* penz. var. *aboparvus*) in 1935.

Failure to infect patients by direct blood inoculation seldom occurs when patients are inoculated at the Clinic, although many failures take place when estrated blood is sent through the post. It is believed that the reason for failures is that most of the parasites die in transit. The incubation period is longer presumably because most of the parasites have died.

Wherever possible, the patients are allowed to have 10 or 12 attacks of fever with temperatures of 104° F. In such cases relapses are few even when infection is induced by mosquito bites. This, it is believed, is because by the end of the fever period most of the patients have become immune. Often the fever is quotidian (*P. vivax*) but this is easily changed to tertian by giving a single intra-muscular dose of neotarsphenamine (75 mgm.) which has a selective destructive action on the half-grown trophozoite.

In the case of the Horton Madagascar strain, compared with the endemic Dutch strain, only half of the dose of this drug is needed to change the fever from quotidian to tertian. It was found that there is a mutual homologous immunity between the Madagascar and the Dutch strains. Even patients who have had natural benign tertian infections in Holland are immune to the Madagascar strain. Primary cases of *P. vivax malaria* usually show two or three days of initial fever. Patients who do not show this initial fever tend to go on to a spontaneous recovery before the desired number of attacks has occurred, owing the ultimate failure to the patient's immunity.

The article concludes with advice to those who employ malaria therapy on the preservation of parasite strains and how to treat the fever after the desired number of attacks has been attained. Reasons are also given why blood films of patients undergoing malaria therapy should be examined frequently during the fever period.

P. G. SHUTE

PITTMAN, P. ROYD M. F. & MEAD, Pauline A. Periodic or Cyclical Recurring Phenomena of Vivax Malaria Infections. *Amer. J. Hyg.* 1947 Sept., v. 46, No. 2, 2-47, 14 figs., 1 refs.]

A statistical analysis was made of data concerning the parasitaemia of 40 white patients with naturally induced *P. vivax* infections (McCoy strain). Each patient experienced a primary attack of at least 3 weeks and a period of latency lasting until the 2nd day after inoculation. Forty patients had recrudescences. 30 had none. The records of each of these two groups were again divided according as to whether the prepatent period ended on an odd or even day. Logarithmic mean parasite counts were computed for each day of the period of observation for each of the four groups, with the data referred first to the day of inoculation and second to the day of first appearance of parasites.

Parasites first appear on an average 1 day after inoculation; the parasite density rises steeply to a peak 1-2 days later and then declines gradually. A significant 12-day cycle was observed in three of the four groups. A 16-day cycle characterized the parasitaemia of 28 patients without recrudescences and with even-day prepatent periods, but when the observed crests of the recurring cycles were synchronized it was found that the parasitaemia of 11 followed 12-day rhythm that 18 followed 16-day cyclical course while that of the remaining six showed no cyclical trend. A significant 16-day cycle was revealed in the parasitaemia of 4 patients extending over 80 days after inoculation.

Either the day of inoculation or of the first appearance of parasites may become the point of reference on which the primary division of patients is made on

the basis of prepatent periods The first paroxysm is not a desirable point of reference

Evidence of brood dominance was afforded by the parasitaemia of 15 patients with even-day prepatent periods and no recrudescences, the mean counts were significantly higher on odd days following inoculation Six of these patients had primary attacks predominantly tertian in character with paroxysms on even days

A statistical study was also made of data concerning recrudescences, and their prior remissions of two days or more, of the 40 patients The purpose of the study was to determine whether the days of onset of recrudescences and remissions follow a rhythmical pattern, whether such pattern is related to the cyclical trend of parasitaemia previously determined, and whether their timing shows dominance in the activity of one brood of parasites over that of the other The data were referred to the day of inoculation, the day of first appearance of parasites, and the day of the first paroxysm of the primary attack

A significant 12-day rhythm was indicated by the days of onset of recrudescences In patients with odd-day prepatent periods the clustering of events was most clearly defined when the onsets were referred to the day of first parasites For patients with even-day prepatent periods the rhythm was most evident when the data were referred to the day of first paroxysm A significant 12-day clustering of remissions was evident only for patients with odd-day prepatent periods

Remissions increase in length as recrudescences grow shorter though no significant correlation between their durations was determined Recrudescences averaged 6.2 and 7.2 days in length for the two groups of patients while remissions averaged 5.8 days for each Thus the length of the two intervals combined was 12 and 13 days respectively

Paroxysms initiating the primary attack and those immediately preceding and following remissions are as likely to occur on odd as on even days, thus affords no evidence of the dominance of one or other brood of parasite

The authors offer no explanation of the cyclical phenomena observed These may be due to some unknown aspects of the schizogonous cycle of the parasites or to intermittent activity of the host's defence mechanism *Norman White*

KULCSAR D D Effect of Malaria on Pregnancy *Canadian Med Ass J* 1947, Oct, v 57, No 4, 332-7 [17 refs]

A study of the effects of malaria on the course of pregnancy, based on admissions from May 1st, 1946 to the end of April 1947 to the Obstetrical Department of the Kweilin Provincial Hospital, the admissions totalling 360 cases The Province of Kwangsi, with its capital Kweilin, is stated to be one of the worst malarial districts in China No accurate data are available, but it is estimated that at least 50 per cent of the population suffer from malaria

In the series under review, 59 cases (17 per cent) showed a positive blood smear on examination, while 173 gave a definite past history of malaria (48 per cent of admissions) Eight patients were treated on clinical signs alone Of 59 patients definitely proved to be positive on blood examination, 19 had premature labour (period of gestation not given) and 9 had threatened or incomplete abortion, i.e. 48 per cent of abnormal cases compared with 18 per cent of abnormalities in the so-called malaria-free group (120) cases

The type of infection in the 59 positive cases was *P vivax*, 26 (44.3 per cent), *P falciparum*, 33 (55.7 per cent), *P malariae*, nil one case of mixed *vivax* and *falciparum* infection From a study of the literature and from

following up some of his cases, the author believes in the occurrence of congenital malaria.

The author thinks that a past history of malaria has no adverse effect on the course of pregnancy except as regards the possibility of recurrent *P. vivax* infections being rather more liable to relapse than *P. falciparum* (55 as compared to 45 per cent.). Of the 59 blood positive cases, 50 were recurrences and only 9 were primary infections. It is thought that most of the recurrences would have been prevented, most of the premature labours continued to term and some of the stillborn infants born alive had suppressive anti-malarial medication been consistently used.

While the author agrees that the most thorough search should be made for any possible cause of fever he suggests that there should be no delay in administration of mepacrine or quinine where there is any clinical suspicion of malaria. Leucopenia and relative monocytosis are regarded as valuable signs of a malarial infection.

The Kahn test was positive in 11 per cent. of cases with positive blood smear or a past history of malaria, as against 7 per cent. in malaria negative cases.

MASON BARR (*Manson's Tropical Diseases* 12th ed. 1945) considers that malaria *per se* is a far more potent oxytocic than any drug. However he recommends care in giving quinine as if it is administered in large doses it may sometimes cause miscarriage but ACTON as cited in the same work, thinks that miscarriage can only be caused by doses of quinine large enough to poison the patient. (The reviewer in the course of a fairly wide experience has come to the same conclusion, in fact he has found that the most efficient abortifacient is a smart attack of subtertian malaria left untreated for a few days.)

Mepacrine was found to be well tolerated by pregnant women in relatively large doses and is replacing quinine in pregnancy although opinions still differ as to its efficacy as compared with the latter drug. With the usual plan of dosage an effective plasma level was found to be attained more rapidly with quinine than mepacrine.

The author treated 30 cases with quinine and 20 with mepacrine. Fifty per cent. of cases treated with mepacrine were controlled after one febrile attack, but only 22 per cent. of those treated with quinine were so controlled. No untoward effects were experienced with either drug but it is considered that paludrine will probably be the drug of choice in the near future. Contrary to previous reports, the author does not think that malaria is a serious predisposing cause of toxæmia.

C. F. Skellern

BELANGADY N. W. Spontaneous Rupture of the Spleen following an Attack of Malaria: Its Causes. *Indian Med. Gaz.* 1947 Sept. v. 82, No. 9 532-41

CHEN G. & GEILING, E. M. H. The Acute Joint Toxicity of Atabrine, Quinine, Hydroxyethylapocuprine, Pamaquine and Pentaquine. *J. Pharm. & Exp. Ther.* 1947 Oct. v. 91 No. 2, 133-9 5 figs

Combinations of quinine and plasmoquine (pamaquin) were used in the treatment of *P. vivax* malaria by STAYOV & BRAD (this *Bulletin* 1929 v. 23 11) soon after the discovery of the latter drug. Atabrine (mepacrine) and plasmoquine were similarly used by MURKINS & FLEMING (this *Bulletin* 1932, 29) in the treatment of malignant tertian malaria. The present author has investigated the acute joint lethal toxicities for mice of certain pairs of the drugs named in the title. Mice of 18 to 20 gm. weight were used in groups of 20 for each test and were injected intraperitoneally with a definite volume of solution based on body weight. It did not materially affect the results whether the two drugs were given in one solution or separately. Deaths were recorded after

an observation period of two days Quinine and atebrin acted independently and similarly as regards toxicity, so also did quinine and hydroxyethyl-apocupreime In the case of atebrin and pamaquin, the lethal effect of the latter was not influenced by a sublethal dose of the former, indicating that the two substances act independently but in different ways The mortality when atebrin was used in the lethal range was, however, greater than expected Quinine with plasmoquine and also quinine with pentaquine (chemically related to pamaquin) displayed a synergistic action as regards toxicity A similar synergistic action of these substances was displayed in their therapeutic action on avian malaria The explanation suggested is that quinine and pamaquin may act on different stages in a vital enzymatic process *J D Fulton*

ELDERFIELD R C KREYSA F J DUNN, J H & HUMPHREYS D D A Study of the Synthesis of Plasmochin by the Reductive Amination Method with Raney Nickel *J Amer Chem Soc* 1948, Jan, v 70 No 1 40-44, 2 figs

BROWN B R & HAMMICK D L A Resolution of Mepacrine [2-Chloro-5-(8-Diethylamino- $\alpha$ -Methyl-Butyl) Amino-7-Methoxyacridine] *J Chem Soc* 1948 Jan 99-100

ANDREWS, W H H, GALL, D & MAEGRAITH, B G Studies on Synthetic Antimalarial Drugs XIX The Effect of Therapeutic Courses of Paludrine on the Relapse-Rate of Vivax Malaria *Ann Trop Med & Parasit* 1947, Dec, v 41, Nos 3/4, 375-9, 1 fig

The relapse rate in *P vivax* infections after administration of a therapeutic course of atebrin (mepacrine) consisting of 200 mgm thrice daily for 2 days followed by 100 mgm thrice daily for 10 days to patients having clinical attacks, was compared with that of two similar groups of patients treated with paludrine The dosages of the latter were 500 mgm twice daily for 14 days and 50 mgm twice daily for 14 days respectively The cases were not specially selected, infection having been acquired by most patients in the Far East and by a few in the Mediterranean A follow-up of 92 cases was made for 6 months, by means of postcards For assessment of results, only those relapses were considered which occurred within this period after treatment The results with paludrine were similar to those obtained by JOHNSTONE [this *Bulletin*, 1947, v 44 284], and the relapse rate was approximately the same on the three different dosage-schedules In a separate experiment, patients were given an initial dose of 10 to 300 mgm paludrine and thereafter 100 mgm weekly for six months The follow-up after treatment was again made by post, cards and microscope slides being provided, the latter were to be returned with a thick blood film if relapse was suspected By this means, the follow-up period for 79 patients was not less than 1 year in each case The total number of relapses was 15, and the relapse rate was lower than those rates which followed the dosage schedules described above *J D Fulton*

CHEN, K K & ANDERSON, R C The Toxicity and General Pharmacology of  $N_1$ - $p$ -Chlorophenyl- $N_5$ -Isopropyl Biguanide *J Pharm & Exper Therap* 1947, Oct, v 91, No 2, 157-60 [10 refs]

The authors have made observations on the pharmacology and toxicity of paludrine in various laboratory animals with results which are summarized as follows

"1 The acute toxicity of  $N_1$ - $p$  chlorophenyl- $N_5$ -isopropyl biguanide HCl has been compared with quinine 2HCl and quinacrine HCl in mice, rats guinea-pigs and rabbits

2. The biguanide has been repeatedly administered in various doses to rats. No pathologic lesions can be demonstrated, and death from large doses may be attributed to acute systemic effects.

3. The biguanide lowers blood pressure with an acceleration of respiratory rate in anesthetized cats.

4. With the exception of the isolated guinea pig's uterus which responds by contraction, the biguanide has an inherently relaxing property on the isolated rabbit's uterus and intestine, and the isolated guinea pig's intestine.

5. The action of the biguanide on the blood sugar of rabbits is suggestive of a slight hypoglycemia."

J. D. Fallon

DEBMARK P. L. Treatment of Relapsing Malaria with Specific Antimalarial Drugs in combination with Penicillin. *Indian Med Gaz* 1947 Sept. A. No. 9 311-14 [13 refs.]

McCORMACK A. & WEBSTER W. Contributions to the Chemistry of Synthetic Antimalarials. Part V. Attempted Synthesis of 6-Methoxy-8-Quinazolinyl-Diethylaminoethylcarbamate. *J. Chem. Soc.* 1948, Jan. 97-9

WYNNE-GRIFFITH G. Suppression of Malaria by Mepacrine. *J. Roy Army Med. Corps.* 1947 Sept. v. 89 No. 3 11-21 5 figs.

This paper relates experiences in Burma during the recent war. The striking fall in malaria morbidity rates that followed the prophylactic administration of mepacrine in 1945 is described. Similar success was achieved among Japanese prisoners of war.

Norman H. Ash

VINE J. M. Malaria Control with DDT on a National Scale—Greece, 1946. [Abridged. *Proc. Roy. Soc. Med.* 1947 Nov. v. 40 No. 13 811-8 (Sect. Epidem. & Stat. Med. 43-50)]

This is a description of a nation-wide attempt that was initiated by UNRRA to eradicate malaria from Greece. DDT was the sole weapon employed. A trial of the ground methods was made in 1945. The resulting fall in malaria incidence and the eradication of insect pests were so satisfactory that the Greek Government allocated £20,000 for the major onslaught in 1946. The organization was based on UNRRA Headquarters at Athens and the Malaria Division of the Athens School of Hygiene. In each of 11 districts into which the country had been divided, there was a Greek malariologist, an American sanitary engineer of the U.S. Public Health Service, Greek sanitary engineers, and Greek inspectors and foremen trained in the technique of preparing DDT mixtures and of spraying. These specialists headed gangs of labourers and trained them to do the actual work. For the eradication of hibernating mosquitoes 5 per cent DDT in either kerosene or Diesel oil was used at 220 mgm. per square foot. In April larvicidal work was commenced. Water accumulations up to 5 kilometres from village or hamlet were sprayed with 5 per cent DDT in Diesel oil. This continued throughout the summer until September 30. Up to November 1 about 10,000 houses and outbuildings were sprayed.

Aeroplanes were used for spraying marsh lands. Eighteen small training planes of the U.S.A.F. trimotor type were employed. The area to be sprayed determined by L.V. survey was 113,000 acres at the beginning of the season. This shrank to 80,000 acres during the dry summer. It was sprayed 3 times. DDT 20 per cent in kerosene was used for all aeroplane work. Under ordinary conditions, pilot could spray about 17 acres per minute.

The side-effects of DDT spraying were interesting. In Athens in 1946 there was an almost total absence of flies. In addition to the spraying of houses, large garbage dumps near the city were sprayed from the air at intervals during the

summer Sandflies disappeared from the Nea Smyrna suburb of Athens. Air-spraying was effective against the *Dacus* fly in olive groves and against a plague of Tene moth in pine and fruit trees. A fall in the notifications of dysentery from July onwards may have resulted from a destruction of flies.

The incidence of malaria was much below the expected level, comprehensive statistical data are not available. It is estimated that some 3,600,000 persons were protected, about 80 per cent of the population at risk. The overall cost per head was two shillings.

An addendum to the paper enunciates the following conclusions and principles —

(1) Comprehensive data on all aspects of the areas to be dealt with are essentially required in advance.

(2) Complete co-operation is required between all sections engaged in the operation, this includes Government, technical and administrative staff and the public, the public must be kept fully informed of developments.

(3) The time-factor of anopheline habits must be taken into account e.g., in Greece *A. elutus* and *A. maculipennis* must be attacked in April, while *A. superpictus* may be overlooked until June–July.

(4) Where possible, blood, spleens and "baby rates" should be studied over typical bad malaria areas before and just after the season.

(5) It is an advantage to make a final onslaught on breeding sites at the end of the season in order to diminish hibernators.

(6) It was found that there was little or no mortality among bees where DDT was used after blossom time. This compares favourably with mortality from other forms of chemical insect controls on fruit and vegetables. On the other hand, when DDT was used in a house where silkworms were breeding, these were inevitably killed.

(7) From experience of 6,000 labourers over six months, it is stated that the toxic effect of DDT on human beings is negligible. The effect on the skin of kerosene and oil must, however, be taken into account.

(8) There are a number of questions still to be answered regarding the activity of DDT, such as the optimum contact time per area, the relative value of larvicidal methods and house-spraying, the best agents for preparing emulsions, the optimum *para-para* content of technical grades of DDT, the effects of temperature and storage, and the most suitable containers for DDT. Much experimental work is still required towards determining the most satisfactory and economic use of DDT in large-scale malaria control schemes.

Norman White

AFRIDI, M. K. & BHATIA, M. L. Malaria Control of Villages around Quetta (Baluchistan) with DDT. *Indian J. Malariology* 1947, June, v. 1, No. 2, 279–87, 1 folding map.

In rural villages in the Quetta district (30°N 67°E) the incidence of malaria is high in the transmission season from mid-July to mid-September. A pilot control scheme in a limited number of villages (20,000 population) was instituted in 1946 with the following aims and objects to find —

(a) Whether malaria in a rural population in Baluchistan could be controlled simply by killing adult mosquitoes by periodic DDT spraying.

(b) Whether the cost *per caput* on such control measures would be within reasonable economic bounds and

(c) Whether spraying operations could be conducted in a community in which the purdah system (seclusion of women) rendered entry into houses difficult.

The villages concerned are described. A 25 per cent DDT emulsion concentrate diluted with 9 parts of water gave a spraying solution containing

2.5 per cent DDT. The dosage applied to wall surfaces was estimated to be 1 to 1.5 cc per sq. ft. (25-38 mgm. DDT per sq. ft.). Three distinct groups of villages were treated once by outdoor spraying; the surfaces treated are not defined between July 22nd and August 2nd, four weeks after this first spraying. One group was re-treated indoors, one group outdoors and one group by a combination of indoor and outdoor spraying. The vector mosquitoes were *A. persectus*, *A. culicifacies* and *A. stephensi*.

A table summarizes the quantities of DDT used and man hours expended. The cost of two sprayings amounted to 2.4 annas per *casah*, but a single insect application of DDT emulsion would be effective for one malaria season at a cost of 1.4 annas exclusive of medical supervision.

The results as assessed by spleen and parasite rates in children in June and September showed a definite effect in lessening the intensity of malaria transmission in two groups of villages whereas in the third group which had been treated by both indoor and outdoor spraying no decrease occurred. This was believed to be due to malaria infections contracted in neighbouring untreated villages. The decrease in spleen rates in the favourable groups were 31 to 38 and 45 to 33 per cent, respectively whereas untreated control villages showed that the usual degree of malaria transmission caused a rise in spleen rate of 36 to 44 per cent between June and September. No insuperable difficulties were encountered in gaining entry into the houses for spraying despite the local pardaish system.

R. Ford T. Dr.

HAWKING F. & HUNT R. The *Locki* Type of Malaria Parasite in Monkeys. *L'et J. bilans J. Roshan* (Soc. Belg. Med. Trop. Brussels) 1947 Dec. 251-461 13 coloured figs. on 2 pls. & 3 figs. 20 refs.]

In the blood of a baboon received from the Gambia a malarial parasite identified as *Plasmodium locki* was found. The parasite occurred as mature gametocytes and ring forms of various sizes. It transpired that the ring forms were immature gametocytes and nothing in the shape of asexual development occurred in the blood. Fresh batches of rings appeared in the blood from time to time. The spherical gametocytes shown on a coloured plate, when mature appear to be extracellular. Batches of *Anopheles quadrimaculatus*, *Anopheles maculipennis*, *Anopheles stephensi*, *Aedes aegypti* and *Culis modestus* were fed on the baboon. Of 771 mosquitoes, a few oocysts were seen in the stomachs of 3 *Anopheles quadrimaculatus* and one *Anopheles maculipennis atroparvus*. With the appearance of GARHAM's description this Bulletin 1947 44 862 of the large schizonts of *P. locki* the authors examined the liver of the infected baboon and found a number of yellow nodules in the liver. These were sectioned and appeared to be degenerated schizonts. Owing to the absence of schizonts from the liver the authors conclude that the parasite is not a *Plasmodium* but a *Haemoproteus*. The paper is illustrated by coloured plates and black and white plates. Large schizonts figured are from Garham's sections and appear.

C. M. Wrenyon

CRUZ W. O. & DE MELLO R. P. Infecção do macaco sul americano sagu (Callithrix jacchus Linnaeus 1758) com o *Plasmodium kneri* [Tsetse flies of the South American Monkey *Callithrix jacchus* with *Plasmodium kneri*] Mem. Inst. Oswaldo Cruz 1947 Mar. 45 N. 1 119-1

The English summary appended to the paper is as follows:—

Infection of the South American monkey Sagu (*Callithrix jacchus* Linnaeus 1758) after inoculation with *Plasmodium kneri* has been observed. Intra-nasal malarial inoculation brings death in about ten days. With intra-muscular inoculation of smaller quantities of parasites spontaneous cure takes



been verified several times. The known 24 hours cycle as well as the morphological characteristics of the *Plasmodium knowlesi* as observed in Rhesus infections, remain the same in the monkey studied.

"The vigor of *Callitrix jacchus* when kept in captivity is definitely less than that observed with Rhesus monkeys, but as its buying cost is thirty times less, it could be considered a useful new experimental animal for malaria research."

MULLIGAN, H W & SOMMERVILLE, T. Malaria in the Malabar Squirrel. *Indian J Malariology* 1947, June, v 1, No 2, 329-35, 30 coloured figs on 1 pl [10 refs]

The authors place on record observations made on a blood parasite of the Malabar squirrel (*Sciurus indicus malabaricus*). The work was interrupted by the 2nd World War and was never completed. [These authors, however, appear to have made further studies on the same parasite, in the course of the Mammalian Malaria Enquiry—see this *Bulletin*, 1947, v 44, 966. They were again unsuccessful in finding exo-erythrocytic stages. In the latter paper the parasite is referred to as *P. ratuifae*.]

The squirrels are found in the dense forests of the Nilgiris, and they live in the upper strata of the trees. Seven out of nine adult animals exhibited the parasites in the blood, chiefly as mature gametocytes. The trophozoites are stated to be scanty and not to occur as small signet-ring forms but occasionally as large rings, later becoming amoeboid and often extremely irregular. No dividing forms were seen either in the blood or in sections of spleen, liver, kidney, lung and intestine. The infected red cells showed no enlargement or stippling. The pigment is dark brown in colour and is very clearly seen in the microgametocyte. This form is characterized by its pale cytoplasm and large nucleus with deeply staining karyosome. Both sexes are slightly larger than the red cell, all trace of which disappears.

The infection appears to be of low pathogenicity, and it is noted that splenectomy failed to heighten the parasitaemia. The infection could not be transmitted by various species of *Anopheles*, *Culex*, *Armigeres* and *Aedes* (*Stegomyia*) mosquitoes. Sub-inoculation of squirrel blood into laboratory animals and monkeys failed to cause infection.

The authors state that this parasite must be identical with that reported from the same locality by Donovan and named by him *P. ratuifae*, they point out that the morphology of the parasite of the Annam squirrel, *P. vassali*, Laveran 1905, is so similar, that a better provisional name for the Indian parasite would be *P. vassali* var. *ratuifae*.

[It seems probable that this haemosporidian belongs to the same category as *H. kochi* of the African lower monkeys [this *Bulletin*, 1947, v 44, 882], *Plasmodium* species of the Palestine bats (MER & GOLDBLUM, *Nature*, 1947, Mar 29, 444), *P. pteropi* of the New Guinea flying foxes [MANWELL, this *Bulletin*, 1947, v 44, 43] and *P. limnotragi* of the Citatunga [VAN DEN BERGHE, *Bull Soc Path Exot*, 1937 v 30, 272]. Exo-erythrocytic schizogony has been described in the first three of these parasites—all in different forms, its discovery in *ratuifae* is awaited with interest.]

P C C Garnham

1 MARSHALL, P B. The Glucose Metabolism of *Plasmodium gallinaceum*, and the Action of Antimalarial Agents. *Brit J Pharmacol* 1948, Mar, v 3, No 1, 1-7, 2 figs [16 refs].

11 ——. The Glucose Metabolism of *Trypanosoma evansi* and the Action of Trypanocides. *Ibid* 8-14, 4 figs [18 refs].

1 The author has investigated the glucose metabolism of *P. gallinaceum* and the effect of antimalarial agents, on lines similar to those of the original

experiments of CHRISTOPHARS & FULTON (this Bulletin 1938, v. 35 709) and subsequent authors whose contributions have been regularly reviewed in the Bulletin. Infected blood from chickens containing 70 to 85 per cent of parasitized cells suspended in isotonic buffer was used in Warburg manometers for the measurement of oxygen uptake. When required, accompanying glucose was removed by washing in the same buffer and the desired substrate or inhibitor added. Phosphorus exchanges were measured in these suspensions over periods of 4 to 5 hours during oxygenation. At the beginning and end of experiments, aliquots of suspensions were deproteinized and after centrifugation the supernatant was analysed for glucose, phosphorylated intermediates, lactic and pyruvic acids. In addition to glucose washed parasitized red cells were able to oxidize glycerol, pyruvate, lactate and to a lesser extent succinate and fumarate. Cyanide and iodoacetic acid acted as inhibitors. Quinine and atabrine (mepacrine) did not appear to be active inhibitors of respiration, and differences in action were noted only at low concentrations of these drugs in presence of various substrates. Phosphorylation of glucose was more marked in parasitized than in normal red cells. The effect of inhibitors and antimalarial agents on phosphorylating reactions was also studied. The author's results did not agree with those of MORTIMER & EVANS (this Bulletin 1946 v. 43 1118) in regard to the use of amino-acids as substrates by the parasite or the nitrogen exchanges brought about by it. A possible pathway for glucose metabolism and mode of interference with it by quinine and mepacrine, is outlined.

II. These experiments on the respiratory metabolism of *T. evansi* have in general confirmed the work of previous authors including that of CHAI & GELLING (Proc. Soc. Exp. Biol. & Med. 1946 v. 63 408) who showed that phosphorylation reactions play a part in the metabolism of glucose by trypanosomes. The experimental methods were similar to those described above. While blood from mice infected with *T. evansi* was used, or in some cases suspensions of the parasite freed from red cells. The effect of a trivalent and a pentavalent arsenical as well as of representative diamidines, on metabolism was investigated. The chief end-product of glucose utilization was pyruvic acid. In the case of trypanosomes freed from blood constituents, mouse plasma caused an increase in respiration possibly because of the presence of certain nutrient factors. When a number of such nutrients, including pantothenate were added to suspensions, no increase in  $O_2$  uptake was, however, observed. As in the case of other trypanosomes, glycerol was metabolized, but not lactate, fumarate, succinate, glutamate or aspartate. Iodoacetic acid and fluoroacetic acid inhibited oxygen uptake but cyanide only to a slight extent. Trypanosomes were active in this respect to varying degrees. Hexokinase is possibly inhibited by trivalent arsenicals. A scheme is outlined for the possible phosphorylation reactions involved during glucose metabolism by the trypanosomes.

(It is surprising to find in the first paper the statement that MAYER & COGGESHALL (1941) showed that parasitized red cells were dependent to some extent on glucose and that mannose, fructose and glycerol would replace glucose as a metabolite. Since the American authors in the paper quoted, write: FULTON (1938) reported that if the blood glucose was removed from the parasite by washing there was a decrease in respiration which could be restored to its former level by the addition of glucose. Fructose, mannose, maltose, or glycerol could be utilized as substitutes for glucose.)

J. D. FULTON

TERMAN L. A. & SUTER L. H. The Effect of Oxygen Tension on *Plasmodium gallinaceum* Malaria in Chickens. *J. Infect. Dis.* 1948 Jan Feb, v. 62, No. 1 1-4 1 fig.

"1. Exposure to oxygen at atmospheric and lower and pressures for periods of 4 to 10 hours daily had no effect on the rate or degree of parasitaemia, the

development of exo-erythrocytic forms, or the survival time of chicks infected with *Plasmodium gallinaceum*

"2 Prolonged daily exposures to oxygen at atmospheric pressure, resulted in a significant decrease in survival time, accompanied during the later stages of the infection by inability of the treated birds to readjust to ordinary air

"3 Oxygen administration, supplemented by quinine therapy, did not alter the course of the infection, and in most cases decreased survival time "

BELTRÁN, E Estudio comparativo de dos plasmodios parasitos de la gallina domestica (*Plasmodium gallinaceum* y *P. juxtanucleare*) [Comparative Study of *P. gallinaceum* and *P. juxtanucleare*] *Rev Inst Salubridad y Enfermedades Trop Mexico* 1947, June, v 8, No 2, 129-38, 1 map [23 refs] English summary

The author compares the two malarial parasites of the fowl—*P. gallinaceum* described by BRUMPT in 1935, and *P. juxtanucleare* first recorded by VERSIANI and GOMES in 1941 [this *Bulletin*, 1942, v 39, 400] from Brazil and by the author in the same year from Mexico. The former is a large parasite producing 24 merozoites and belongs to the Old World, while the latter is a small parasite giving rise to 4 merozoites. The data available for *P. juxtanucleare* are very incomplete, as it has been little investigated. C M Wenyon

MICKS, D W A Loss of Gametocytes in *Plasmodium elongatum* *J Parasitology* 1947, Dec, v 33, No 6, 499-505, 2 figs [12 refs]

A strain of *P. elongatum* which had been maintained, since its isolation from a field sparrow, in canaries (10 passages) and ducks (10 passages) and which gave a parasite rate of 3.6 infected cells per 100 red corpuscles (90 per cent of the parasites being gametocytes) was subinoculated to canaries. After 5 further passages of the duck strain (15 in all) and 4 passages of the canary strain, both strains became free from gametocytes. The two strains free of gametocytes were carried on through many duck and canary passages, but they never returned to normal. Inoculation to a sparrow produced no change. Two other strains started in ducks from canaries and the original canary strain ran a normal course. C M Wenyon

## BLACKWATER FEVER

DAWSON, J & FINDLAY, G M Experiments on the relation of Haemoglobinuria and Anuria with reference to Blackwater Fever *Ann Trop Med & Parasit* 1947, Dec, v 41, Nos 3/4, 306-20 9 graphs [18 refs]

This very interesting paper records the results of experiments designed to determine the effects of injection of haemoglobin or its derivatives in dogs and monkeys.

Injection of 3 gm homologous haemoglobin depressed glomerular filtration rate (measured by inulin clearance) slightly in normal dogs and to a much greater degree in dogs which had been bled severely eighteen hours before the injection. The urinary flow was not affected in normal dogs, in the bled animals it was greatly diminished and in some cases ceased. Serial counts of "blocked" tubules in renal tissue showed there was no correlation between the extent of tubular blocking and the clinical result of the injection. On the other hand, the glomerular capillaries were empty in 78 per cent of the bled dogs and

in only 32 per cent. of the normal animals. The authors concluded that impairment of the glomerular filtration and not blocking, was the basis of the interference with urinary flow and that filtration was much more seriously affected in the animals which had been subjected to haemorrhage. The oliguria, anuria and reduction in toxin clearance were related to lack of blood supply to the glomeruli as previously postulated by MACGRAITH and HINDLAY (*this Bulletin* 1945 v 4, 12).

The effect of injection of haemoglobin on the blood pressure of dogs was measured directly and it was demonstrated that whereas little change was observed in normal animals, in dogs which had previously been bled, a rise in blood pressure occurred after haemoglobin injection. This rise of blood pressure could be correlated with the absence of blood from the glomerular capillaries. Further experiments showed that from 60 to 90 minutes after injection of haemoglobin into anaemic animals a pressor substance could be extracted from the circulating blood. This substance was not present in blood from injected normal animals. Its production appeared in some way to be related to diminution of the oxygen-carrying power of the blood.

As a result of the chance observation that histidine output in the urine increased for 4 hours after transfusion in a case of toxæmia of pregnancy the output of this amino-acid was estimated in cases of haemoglobinuria in Africans. No obvious correlation was noted between the output of histidine and haemoglobin. In one case of haemoglobinuria which was almost anuric however the histidine excretion was greatly increased during the period of lowest urinary output. Blood removed immediately after the death of this patient was extracted in the same way as the dog's blood and found to contain a pressor substance.

Working on the hypothesis that the pressor substance might be developed in a manner similar to angiotensin, which contains histidine the authors attempted to prepare a pressor substance (peptensin) with the use of haemoglobin as a substrate and commercial pepsin as the enzyme. The pressor activity of the extract was not constant. If the extract had low free histidine content it was active; if rich in histidine it was inactive.

The authors suggest that failure of histidine excretion in a patient during intravascular haemolysis may be due to the development of some pressor substance in the blood. On the analogy of the renal angiotensin system, renal anoxia (arising from anaemia) might promote the appearance of an enzyme capable of acting on the globin of haemoglobin to produce a pressor substance possibly a polypeptide. This would constrict the glomerular vessels increase the degree of renal anoxia and diminish the glomerular filtration rate.

B. G. Macgrath

HARRISON H. E. BUNTING H. ORLWAY N. H. & ALBRITCK W. C. The Pathogenesis of the Renal Injury produced in the Dog by Hemoglobin or Methemoglobin. *J. Exper. Med.* 1947 Oct 1. 80 v 4 339-54. 6 text fig. & 6 figs (1 coloured) on 3 pls. 23 x 1.

This paper deals with the pathogenesis of renal dysfunction in dogs resulting (1) from intravascular haemolysis occurring after passive (artificial) and (2) from intravenous injection of solutions of homologous haemoglobin and methemoglobin. Kidney function was studied by serial estimations of blood urea & plasma creatine and creatinine clearances. Filtration fluid through the glomerular membrane was determined by intra-arterial administration of ferricyanide and subsequent examination of frozen kidney sections. Direct measurement of renal blood flow was made in two dogs in which one kidney was brought to the flank under anaesthesia without tension on the pedicle.

Dogs were found to be resistant to the injurious effects of intravascular haemolysis after exposure to arsine, renal injury was apparent only in cases of extreme haemolysis. Injection of solutions of haemoglobin affected renal function only when the dosage was large. Small doses of haemoglobin injected into four animals made oliguric by deprivation of water caused no appreciable change in plasma urea N. Larger doses in oliguric dogs produced temporary anuria and changes in endogenous creatinine clearance.

The authors quote BING's results (*Bull. Johns Hopkins Hosp.*, 1944, v 71, 161) which showed that severe renal injury followed injection of methaemoglobin in dogs rendered acidotic with ammonium chloride, whereas injection of methaemoglobin or comparable amounts of haemoglobin in normal animals had little effect. They determined the effects of injection of methaemoglobin in normal dogs, dogs made oliguric by deprivation of water, and dogs rendered "acidotic" by intragastric injection of 0.1 N hydrochloric acid.

In non-acidotic dogs with good urinary flow, injection of methaemoglobin in doses of 1 gm per kilo had no effect on renal function. The same dosage in oliguric non-acidotic dogs had serious effects in some cases, including temporary or permanent anuria. In acidotic dogs, in which the urinary output was high, injection of methaemoglobin appeared to have little deleterious effect, in the one animal for which details are given, it produced a temporary diuresis. The authors conclude that in these acidotic animals "although acidosis probably did have some effect in increasing the kidney damage the rate of urine flow was the more important."

Creatinine clearances were measured in some dogs before and after injection of haemoglobin and methaemoglobin. Representative figures are given in text tables.

Injection of haemoglobin in doses of about 4 gm/kilo into two oliguric dogs produced immediate almost complete stoppage of urinary flow. In one animal, this period of anuria was of short duration and was followed by a great increase of urinary flow, up to seven times greater than during the original oliguric state, twenty hours later, the urinary flow was still twice what it had been before injection. Endogenous creatinine clearance was reduced in this dog to two-thirds 60 minutes after the injection and to one-half of the initial figure twenty hours later. In the second dog, there was no post-anuric diuresis and the urinary flow was about double the initial flow twenty hours after the injection, creatinine clearance fell to a trace after the injection and twenty hours later was still only one-sixtieth of the original level.

Injection of methaemoglobin in doses of about 1 gm/kilo into two oliguric dogs produced anuria in both. This persisted in one animal, but in the other urinary flow was restored to the pre-injection level after 90 minutes. In the anuric dog, the creatinine clearance was reduced to a trace. In the other animal, it fell to about one-fiftieth of the original figure about 100 minutes after the injection and was only one-eighteenth four hours later, although the urinary flow had been re-established.

In the one acidotic dog for which details are given, the same dose of methaemoglobin produced a diuresis associated with a reduction of creatinine clearance in the first hour after injection. Subsequently the urinary flow continued at a slightly greater rate than before the injection, but the creatinine slowly fell to one-fifth of the initial figure.

It will be seen from these figures that there appeared to be little relation between the prevailing urinary flow and the endogenous creatinine clearance. Nevertheless, the authors considered the possibility that "a marked reduction of renal blood flow" occurred after the injection of the pigments. They measured renal venous flow directly in two oliguric animals injected with a dose of 1 gm methaemoglobin per kilo. No evidence of reduction of (total)

renal blood flow was found in either animal except after "prolonged anaesthesia and manipulation.

Histological changes in the form of eosinophilic granular precipitates in the glomerular spaces and lumina of the tubules were found within a few hours of the onset of haemoglobinuria in dogs exposed to aniline or injection of haemoglobin or methaemoglobin. With 4 hours of exposure to aniline and two hours after injection of the pigments "masses of granular yellow brown refractive material and well formed casts were found in the loops of Henle distal convoluted tubules and collecting tubules. In severe cases of haemoglobinuria, hyaline eosinophilic droplets which the authors considered to be haemo-labes were found in the epithelium of the proximal convoluted tubules. By 36 to 48 hours after the onset of haemoglobinuria, coagulative necrosis of the epithelium of some of the proximal convoluted tubules was evident. Later signs of regeneration of epithelium appeared and granules containing free iron were found in the epithelial cells. After 3 or 4 days "radial zones of tubules containing casts, alternating with sections free of casts" (often with dilated tubules) were seen. Injection of ferrocyanide showed that filtration through the glomerular membrane had occurred even in apparently blocked tubules. The material filling the lumina of the tubules was identified as mainly methaemoglobin in concentrated solution of gel-like consistency. The number of casts per unit area of cortex and medulla was determined. The degree of impairment of renal function was greatest in those animals in which casts were most numerous, and least in those in which casts were few. In four animals, renal insufficiency was present in association with only a small number of casts and in these no anatomical basis for impaired function was found.

The authors conclude that severe and persistent impairment of kidney function results in dogs from intra-vascular haemolysis after exposure to aniline and from intra-venous injection of solutions of homologous haemoglobin and methaemoglobin. They consider the evidence presented in their paper shows that obstruction to urinary flow through the tubules is an important factor in the early reduction of kidney function. The material in the lumina was a concentrated solution of methaemoglobin and there was no evidence of the formation of pigment insoluble at the pH of urine (after methaemoglobin injection the pH of the urine rose in some animals at the beginning of haemoglobinuria). Injury to the epithelium of the proximal convoluted tubules occurred last after injection of methaemoglobin haemoglobin or following exposure to aniline. Such epithelial damage probably contributed to the persistent severe depression of renal function.

Direct measurement of renal venous flow in two dogs did not confirm the observation of other workers who held that injection of haemoglobin caused reduction in renal blood flow. (In these experiments the authors injected methaemoglobin.)

(In coming to their conclusions, the authors have had the advantage over the reader in that they have had access to all the protocols of experiments. The information provided in the text is often inadequate. For instance, the table illustrating the correlation between the number of casts, histological changes in the proximal tubules and evidence of impairment of renal function, gives no indication of the dose of aniline or methaemoglobin used. It is thus not possible to see what relation existed between the dose and the severity of the lesions, which considerably weakens the argument. Similarly the evidence provided concerning changes in creatinine clearance is insufficient and inadequate from the point of view of the conclusions drawn. In the experiments quoted in the tables there appears to be little relation between rate of urinary flow and the changes in creatinine clearance. The acknowledgment that the urinary flow was an important factor in modifying the effects of methaemoglobin injection

in acidotic dogs, might be a useful argument in favour of the view that the pathogenesis of renal injury of this kind is related to the glomerular blood flow

The two experiments in which renal blood flow were measured show a reduction in total flow some time after the injection of methaemoglobin, in one case after the re-establishment of oliguric flow, in the other during anuria. It is possible to interpret these results as the authors have done, provided the surgical interference and transposition of the kidneys is disregarded, in terms of no reduction in renal flow following the injection. It should be noted, however, that this refers only to total flow and has no reference to the flow through the cortex, which, for all the evidence provided here, may as well be shunted to the medulla as not. This paper leaves us much where we were.]

B G Maegrath

KHO LIEN KENG Een geval van zwartwaterkoorts met cyanose (methaemoglobinaemie), waarschijnlijk door plasmochine [**Blackwater Fever and Cyanosis of Plasmochine Origin**] *Med Maandblad Batavia* 1948, Jan, No 18, 342-7 [30 refs]

Plasmochine has certain advantages by its gametocidal action in malaria therapy, but is undoubtedly toxic. The problem of the cause of blackwater fever is linked in the literature with malaria, quinine and plasmochine. It is now more than twenty years since plasmochine was announced (1926) as a drug for use and, in the light of what is now known of its toxic character, it is astonishing to learn that, originally, it was given in a dose of even 250 mgm daily. The present article gives a useful historical account of the subject as introduction to the author's own case of blackwater fever with cyanosis (methaemoglobinaemia). The patient was a young Chinese of 17 years who came for consultation with fever which had started the day before. It was not surprising that as he lived in Batavia and suffered regularly from 3 to 4 attacks of malaria every year, a blood film showed the presence of tertian malaria schizonts. He was given a prescription for 300 mgm. quinine bisulphate four times daily for five days and the temperature fell immediately. Five days after stopping treatment the fever, in this subject of chronic malaria, recurred and he was now given 300 mgm quinine together with 10 mgm plasmochine, both three times daily. Four days later he reappeared still with fever, looking cyanotic and passing dark red urine. Other symptoms were vomiting, headache, cough and general malaise but no enlargement of the spleen. The blood serum was dark brown and gave the spectrum of methaemoglobin only, oxy- and sulphaemoglobin being excluded. There was no direct van den Bergh reaction, but the indirect reaction was obtained on two occasions. After the patient's admission to hospital, the haemoglobinuria lasted 3 days, the cyanosis a week and jaundice 10 days. His temperature fluctuated between 102° and 105.8°F and he was occasionally delirious. A thick blood film showed no parasites. No albumin, no sugar, but much urobilin were present in the urine. Treatment consisted of vitamins, fruit and fluid. Diuresis was good. A blood transfusion of 250 ml was followed by a pyrexial reaction.

Differential diagnosis lay between blackwater fever and plasmochine toxæmia. "It is not improbable that sensitization by previous malarial attacks and plasmochine poisoning are contributory to the development of blackwater fever."

W F Harvey

renal blood flow was found in either animal except after "prolonged anaesthesia and manipulation.

Histological changes in the form of eosinophilic granular precipitates in the glomerular spaces and lumina of the tubules were found within a few hours of the onset of haemoglobinuria in dogs exposed to aniline or injection of haemoglobin or methaemoglobin. With 4 hours of exposure to aniline and 10 hours after injection of the pigments "masses of granular yellow brown refractive material and well-formed casts" were found in the loops of Henle distal convoluted tubules and collecting tubules. In severe cases of haemoglobinuria, hyaline eosinophilic droplets which the authors considered to be haemoglobin were found in the epithelium of the proximal convoluted tubules. By 36 to 48 hours after the onset of haemoglobinuria, coagulative necrosis of the epithelium of some of the proximal convoluted tubules was evident. Later signs of regeneration of epithelium appeared and granules containing free iron were found in the epithelial cells. After 3 or 4 days "radial zones of tubules containing casts, alternating with sections free of casts (often with dilated tubules) were seen. Injection of ferrocyanide showed that filtration through the glomerular membrane had occurred even in apparently blocked tubules. The material filling the lumina of the tubules was identified as mainly methaemoglobin "in concentrated solution of gel-like consistency. The number of casts per unit area of cortex and medulla was determined. The degree of impairment of renal function was greatest in those animals in which casts were most numerous and least in those in which casts were few. In four animals, renal insufficiency was present in association with only a small number of casts and in these no anatomical bases for impaired function was found.

The authors conclude that "severe and persistent impairment of kidney function results in dogs from intravascular haemolysis after exposure to aniline and from intravenous injection of solutions of homologous haemoglobin and methaemoglobin. They consider the evidence presented in their paper shows that obstruction to urinary flow through the tubules is an important factor in the early reduction of kidney function. The material in the lumina was a concentrated solution of methaemoglobin and there was no evidence of the formation of pigment insoluble at the pH of urine (after methaemoglobin injection, the pH of the urine rose in some animals at the beginning of haemoglobinuria). Injury to the epithelium of the proximal convoluted tubules occurred late after injection of methaemoglobin, haemoglobin or following exposure to aniline. Such epithelial damage probably contributed to the persistent severe depression of renal function.

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In coming to their conclusions the authors have had the advantage over the reader in that they have had access to all the protocols of experiments. The information provided in the text is often inadequate. For instance the table illustrating the correlation between the number of casts, histological changes in the proximal tubules and evidence of impairment of renal function, gives no indication of the dose of aniline or methaemoglobin used. It is thus not possible to see what relation existed between the dose and the severity of the lesion, which considerably weakens the argument. Similarly the evidence provided concerning changes in creatinine clearance is insufficient and inadequate from the point of view of the conclusions drawn. In the experiments quoted in the tables there appears to be little relation between rate of urinary flow and the changes in creatinine clearance. The acknowledgment that the urinary flow was an important factor in modifying the effects of methaemoglobin injection



the most ambitious example—it is briefly described in the present paper, on the lines of the previous description given by the author [see this *Bulletin*, 1946, v 43, 1022]. The basic policy for control in Nigeria is mass treatment, dispensary follow-up, and clearance by communal effort. The effect of insecticidal methods has not yet been investigated on a large scale.

Charles Wilcocks

VAUCEL, M & CECCALDI, J. Les anciens trypanosomes se re-infectent-ils ? [Do Former Patients with Trypanosomiasis become infected a Second Time ?] *Liber Jubilare J Rodhain (Soc Belge Méd Trop, Brussels)* 1947, Dec, 395-409 [10 refs]

Four patients are described who were discovered during a routine examination to be infected with trypanosomes. Their general clinical condition was good and there was no evidence of infection of the nervous system. They were treated with atoxyl, tartar emetic or Fournieu 270 and followed up by examinations every 6 months. After 8 to 12 years they were found to be infected once again, but the infections responded readily to the usual treatments. Three other patients, who had applied for treatment owing to their symptoms, were treated with atoxyl-tartar-emetic, trypanamide or Fournieu 270. Five to eight years later, they were found to be infected again, they responded readily to further treatment. The interpretation of these cases is discussed. Five or more of the patients may have been reinfected. On the other hand, all the cases may represent reactivation of the infection after a prolonged latent period. The evidence is insufficient to decide which of these interpretations is correct.

F Hawking

BUCK, Margaret. Persistence of the Parabasal Body in a *p*-Rosaniline Resistant Strain of *Trypanosoma brucei*. *Proc Soc Exper Biol & Med* 1948, Jan, v 67, No 1, 77-9, 1 fig.

"A *p*-rosaniline-resistant modification of *T. brucei* is described in which—contrary to the experience with other trypanosome strains—the parabasal body persisted. The strain also failed to show the overlapping resistance to 6,6'-ureylene [4-amino-2-methyl-quinolone] which could be demonstrated in *p*-rosaniline-fast strains of *T. equiperdum*."

VAN HOOFF, L, HENRARD, C & PEEL, E. Observations sur le *Trypanosoma brucei* produisant des infections naturelles dans une région infestée de *Glossina palpalis*, en l'absence de *G. morsitans*. [Observations on *T. brucei* producing Natural Infections in a *Glossina palpalis* Region, in the absence of *G. morsitans*] *Liber Jubilare J Rodhain (Soc Belge Méd Trop, Brussels)* 1947, Dec, 359-80 3 figs [11 refs]

Description of three strains of *T. brucei*, from natural infections in a dog, pig and goat, isolated in the western region of the Belgian Congo, where the only important vector is *Glossina palpalis*. With these strains cyclical and mechanical passages were carried out through various mammals, including man.

Both in natural and experimental infections of pigs, *T. brucei* was more abundant in the blood than in the case of *T. gambiense* infections, the number of parasites gradually diminishing until the animals recovered spontaneously after periods up to 15 months. Attempts to reinfest the pigs with *T. gambiense* failed but were successful with *T. rhodesiense*. It is suggested that in *palpalis* areas the pig probably serves as a reservoir of *T. brucei*. In goats, *T. brucei* produced acute or subacute infections, terminating fatally in from one to seven months, with symptoms of encephalitis. In dogs the infection ran an acute or subacute course, with the characteristic symptoms of keratitis, on account of

## TRYPANOSOMIASIS

McLITCHIE J. L. The Control of Sleeping Sickness in Nigeria. *Trans. R. Soc. Trop. Med. & Hyg.* 1949, Jan., v 41 No. 4 443-70 4 maps & 9 figs. [35 refs.] Discussion 471-60 [HOLLINS C. TONDO K. W. RAE, WILSON DUGGAN A. J. BUXTON P. L. CHESTERMAN C. C. MACKENZIE, G. MANSON BARR, P. McLITCHIE (in reply)]

The author has divided his account of the control of sleeping sickness in Nigeria into several parts: the distribution of tsetse flies, drug resistance of trypanosomes, incidence of the disease, characters of the disease, treatment, prophylaxis and control. The paper therefore contains more than its title indicates, and is in fact, a very comprehensive statement of the whole position, written by a man who has been very actively implicated in the work.

The earlier sections of the paper are themselves largely accounts of work done and opinions expressed by other people. The vectors are *Glossina palpalis* and *C. lukwinda*; the trypanosome is *T. gambiense* which gives rise to three categories of disease: mild and scanty blood infection, moderately virulent, invading the nervous system in 6-12 months, severe (like the Rhodesian form) but only feebly transmissible. These have been described before by LEISTNER.

In Nigeria and other West African countries, sleeping sickness was considered to be quiescent and sporadic before 1925, but about that time there occurred a great increase in incidence, which was due not to the spread of tsetse but to dispersal and free movement of the population. Survey teams were organized in 1930 and in the first five years found an incidence of 13.6 per cent. in 1½ million persons examined. In some places the rate was up to 20 per cent. In the next five years the extent of the infected areas was more clearly defined, and the average incidence was 8.6 per cent. In the last period—of 8 years—the incidence in new surveys was 1.5 per cent.

McLitchie stresses the point made by several authors, that even in areas in which the type of sleeping sickness is apparently mild, and in which the infected persons appear to be in good health, the death rate is high. The mild disease may be only slowly progressive as regards involvement of the nervous system, but sudden breakdown with high fever and anaemia occurs and is apparently relatively common. The trypanosome of low virulence is specially associated with epidemics being easily transmissible. On the other hand, true mild cases do occur in which infection persists for years, the patient and the parasite being in a state of equilibrium.

Treatment varies according to conditions, but a combination of antypol (0.5 gm.) and trypanamide (1.5 gm.) is becoming more common. This combination is given at intervals of 5 days for 6-20 injections according to severity. Pentamidine (intramuscularly) can replace antypol, and can be given at the same time as trypanamide. One intensive course, for use in small remote groups, consists of pentamidine isethionate 100 mgm. the first day, followed by 200 mgm. daily to the seventh day, together with trypanamide injections to a total of 6-9 gm. in the same seven days or in ten days. Pentamidine is also used as a prophylactic.

In control, the first step has been mass treatment and this was essential in the face of epidemics. Since 1931 half a million patients have been treated, most during surveys and at dispensaries, but over 50,000 at general medical stations. The incidence rate in populations examined, which rose to 20.5 per cent. in 1935, was in 1945 down to 1.7 in new surveys. The dispensaries are popular.

Control of tsetse comprises protective clearing, of streams (rod clearing) and aggressive clearing, of large areas. Of the latter the Anchoa corridor is

conveyed mechanically by other biting flies, particularly tabanids, when the time between two successive bites is very short, there is little doubt that this occurs in herds of animals in tsetse-free areas of Africa though, as these are situated near to tsetse-infested areas, the long establishment of infection by mechanical transmission alone is difficult to prove. In countries far from Africa, however, such as Mauritius, the West Indies, Central America and South America, where no tsetse flies exist and where infection with *Trypanosoma vivax* among domestic animals has become a serious problem, it must be concluded that the disease is spread by mechanical transmission by biting flies. Other tsetse-borne pathogenic trypanosomes, imported into tsetse-free areas, have caused outbreaks of disease in animals, but the infections have not become established there.

These facts arouse interest in the question of the relationship of *T. brucei* to *T. evansi*, the latter is monomorphic and indistinguishable in appearance from the long, thin forms of *T. brucei*, but some strains of *T. evansi* show polymorphism and even posterior-nuclear forms, yet in experiments they failed to infect tsetse flies. Laboratory strains of *T. brucei*, maintained by syringe-passage, eventually become monomorphic, the long, thin forms alone persisting, and lose their power of developing in tsetse flies. It was found also that strains of *T. vivax* in tsetse-free countries (Ruanda and Martinique) could not develop in tsetse flies. It is suggested, therefore, that *T. evansi* has arisen from *T. brucei*, camels may have been infected with *T. brucei* during visits to tsetse-infested areas and on their return to the Sudan the infection was spread mechanically by tabanids, became established and was carried in caravans to Asia and elsewhere. An alternative suggestion that *T. brucei* was originally *T. evansi* cannot be excluded. [The articles in the list of references have nearly all been abstracted in this *Bulletin* from 1930 onwards.] J F Corson

HOPPE, J O & CHAPMAN, C W. Rôle of Glucose in Acute Parasitemic Death of the Rat Infected with *Trypanosoma equiperdum*. *J Parasitology* 1947, Dec, v 33, No 6, 509-16, 1 fig [19 refs]

Rats infected with *T. equiperdum* by intraperitoneal injection of 2 million trypanosomes survived 90.65 ± 34 hours. During the infection, the blood sugar decreased from a normal of 145.6 milligrammes per cent to 32.8 milligrammes per cent at the time of death. The sugar remained at the normal level for the first 48 hours, then decreased by 1 per cent per hour up to 72 hours and finally by 3 per cent per hour to the death of the animal. At the time of death, the trypanosomes numbered 1.566 million per cmm of blood. If 5 gm of glucose per kgm of body weight was administered orally every three hours, commencing shortly before the expected death of the rat, life would be prolonged on an average 18 hours, the trypanosomes reaching 3.744 million per cmm of blood. The rats at 48 hours of the infection survived doses of insulin not greater than 5 units per kgm, while normal rats survived 400 units per kgm. From the authors' observations, the conclusion is reached that hypoglycaemia is the cause of death in albino rats infected with *T. equiperdum*. C M Wenyon

See also p 495, MARSHALL, The Glucose Metabolism of *Trypanosoma evansi*, and the Action of Trypanocides

CHEN, G & MCCREARY, J H. An Evaluation of Assay Methods for Arsenicals. *J Pharm & Exper Therap* 1947, Oct, v 91, No 2, 140-43, 1 fig

Chen *et al* previously described an *in vivo* and an *in vitro* method for the assay of trypanocidal activity of antimonials [this *Bulletin*, 1945, v 42, 869,

which the dog may serve as a test animal for differentiating *T. brucei* from the human trypanosomes. The behaviour of *T. brucei* in monkeys and the susceptibility of *Cercopithecus* was low; the infection running a symptomatic course with spontaneous recovery. *Cercopithecus* was highly susceptible; the course of the disease being acute and fatal.

The index of transmissibility of the porcine and caprine strains of *T. brucei* by *G. palpalis* was higher than that of *T. gambiense*. It was found that passage through *Cercopithecus* considerably increased its transmissibility. Twelve flies fed on cultures maintained for 8 months became infected and were able to transmit the infection cyclically to guinea-pigs.

Since a chronic infection correlated with a high degree of transmissibility was an ideal condition for the maintenance of endemicity, it is thought that in the region under consideration, where game is scarce, the best reservoir host of *T. brucei* is provided by the pig.

Treatment with various drugs showed that *T. brucei* was fairly resistant to trypanamide about 0.3 gm. per kgm. being required to effect a cure in guinea-pigs. As regards tartar emetic 3 injections of 0.05 gm. was the curative dose for dogs while guinea-pigs required 1.0 gm. per kgm. combined with 0.015 gm. per kgm. of Bayer 205. The latter drug produced the best results in doses of 0.05 gm. per kgm. against all three strains. On the other hand, Surfen C was ineffective.

Normal human serum had a pronounced trypanocidal action on all three strains. *T. brucei* 3-8 cc. causing the disappearance of the trypanosomes from the blood in guinea-pigs, while 1 cc. had a prophylactic effect. This trypanosome was made serum-resistant by administering progressively increasing subcutaneous doses, until resistance to 100 cc. was produced in guinea-pigs.

The pathogenicity of *T. brucei* to man was tested by cyclical transmission to seven volunteers of the canine and caprine strains, from the natural hosts, after passages through domestic animals, and after rendering the trypanosomes resistant to human serum. All these attempts, except one, failed. In the positive case trypanosomes were seen in a thick blood film of the volunteer three weeks after the infective bites by tsetse, but subsequent examinations of the blood and cultures were negative and inoculation of the blood to other animals produced no infection.

The human experiments were designed to elucidate the role of *T. brucei* in the genesis of acute cases of sleeping sickness of the holoenzootic type which occur in *gambiense* areas in the presence of *G. palpalis* vectors. The single positive case represents a transient infection in a person who was exceptionally susceptible to the infection. The authors suggest that among numerous persons exposed to the bites of tsetse-flies infected with *T. brucei* the susceptibility of some individuals might occasionally be still greater, the infection lasting long enough to allow the flies to feed again, an infection and transmit it further. In this way there might be produced a mutant strain of *T. brucei* which would adapt itself to the new host.

The existence of cross-immunity between *T. brucei* and *T. gambiense* points to the presence of group antigens in the polymorphic trypanosomes. It is suggested that the relationship between these trypanosomes could be tested by attempting to transform *T. gambiense* into *T. brucei* resistant to dogs or goats.

C. A. Hume

HUANG, C. A. Tsetse-borne Trypanosomiasis outside their Natural Boundaries. *Laboratoire J. Rudet (Soc. Belg. Méd. Trop. Brussels)* 1947 Dec. 267-77. 28 refs.

It has been shown experimentally that pathogenic trypanosomes of man and animals in Africa which are cyclically transmitted by tsetse flies can also be

conveyed mechanically by other biting flies, particularly tabanids, when the time between two successive bites is very short, there is little doubt that this occurs in herds of animals in tsetse-free areas of Africa though, as these are situated near to tsetse-infested areas, the long establishment of infection by mechanical transmission alone is difficult to prove. In countries far from Africa, however, such as Mauritius, the West Indies, Central America and South America, where no tsetse flies exist and where infection with *Trypanosoma vivax* among domestic animals has become a serious problem, it must be concluded that the disease is spread by mechanical transmission by biting flies. Other tsetse-borne pathogenic trypanosomes, imported into tsetse-free areas, have caused outbreaks of disease in animals, but the infections have not become established there.

These facts arouse interest in the question of the relationship of *T. brucei* to *T. evansi*, the latter is monomorphic and indistinguishable in appearance from the long, thin forms of *T. brucei*, but some strains of *T. evansi* show polymorphism and even posterior-nuclear forms, yet in experiments they failed to infect tsetse flies. Laboratory strains of *T. brucei*, maintained by syringe-passage, eventually become monomorphic, the long, thin forms alone persisting, and lose their power of developing in tsetse flies. It was found also that strains of *T. vivax* in tsetse-free countries (Ruanda and Martinique) could not develop in tsetse flies. It is suggested, therefore, that *T. evansi* has arisen from *T. brucei*, camels may have been infected with *T. brucei* during visits to tsetse-infested areas and on their return to the Sudan the infection was spread mechanically by tabanids, became established and was carried in caravans to Asia and elsewhere. An alternative suggestion that *T. brucei* was originally *T. evansi* cannot be excluded. [The articles in the list of references have nearly all been abstracted in this *Bulletin* from 1930 onwards.] J. F. Corson

HOPPE, J. O. & CHAPMAN, C. W. Rôle of Glucose in Acute Parasitemic Death of the Rat infected with *Trypanosoma equiperdum*. *J. Parasitology* 1947, Dec., v 33, No 6, 509-16, 1 fig. [19 refs.]

Rats infected with *T. equiperdum* by intraperitoneal injection of 2 million trypanosomes survived 90.65 ± 34 hours. During the infection, the blood sugar decreased from a normal of 145.6 milligrammes per cent to 32.8 milligrammes per cent at the time of death. The sugar remained at the normal level for the first 48 hours, then decreased by 1 per cent per hour up to 72 hours and finally by 3 per cent per hour to the death of the animal. At the time of death, the trypanosomes numbered 1.566 million per cmm of blood. If 5 gm of glucose per kgm of body weight was administered orally every three hours, commencing shortly before the expected death of the rat, life would be prolonged on an average 18 hours, the trypanosomes reaching 3.744 million per cmm of blood. The rats at 48 hours of the infection survived doses of insulin not greater than 5 units per kgm, while normal rats survived 400 units per kgm. From the authors' observations, the conclusion is reached that hypoglycaemia is the cause of death in albino rats infected with *T. equiperdum*. C. M. Wenyon

See also p. 495, MARSHALL. The Glucose Metabolism of *Trypanosoma evansi*, and the Action of Trypanocides.

CHEN, G. & MCCREARY, J. H. An Evaluation of Assay Methods for Arsenicals. *J. Pharm. & Exper. Therap.* 1947, Oct., v 91, No 2, 140-43, 1 fig.

Chen *et al.* previously described an *in vivo* and an *in vitro* method for the assay of trypanocidal activity of antimonials [this *Bulletin*, 1945, v 42, 869, (329)].

1946, v. 43 315]. The former was based on the suppressive and curative activity of the drugs in *T. speridernum* infections of mice and the latter on the interference with glucose metabolism of the isolated trypanosomes. Similar methods have now been used for evaluating arsenicals. In addition, the concentration of various drugs which caused death of the trypanosomes over an observation period of one hour was determined in coverslip preparations of infected blood mixed with Ringer Locke solution. The results obtained by the two *in vivo* methods agreed well among themselves and also with those based on interference with glucose metabolism in the case of trivalent compounds. When potencies were estimated by comparing lethal concentrations of the substances in coverslip preparations, the results were not in harmony with those of the other tests. The authors consider that the suppressive method of estimating trypanocidal potencies of arsenicals is satisfactory. The *in vivo* method, based on interference with glucose metabolism by the trypanosomes, has advantages for certain classes of arsenicals on account of its simplicity.

J. D. Fuller

FLOCH H. La maladie de Chagas au Guyane française [Chagas's Disease in French Guiana.] *Institut Pasteur de la Guyane et du Territoire de l'Inim.* Publication No. 161. 1947 Nov. 5 pp. [13 refs.]

FLOCH H. & CAMARÉ R. Deux nouveaux cas de maladie de Chagas. Guyane française [Two New Cases of Chagas's Disease in French Guiana.] *Institut Pasteur de la Guyane et du Territoire de l'Inim.* Publication No. 162. 1947 Sept. 4 pp.

PELLEGRINO J. & MESQUITA, S. S. A reação de fixação do complemento na doença de Chagas. I.—Nota sobre falsas reações positivas e dúvidas feitas com antígeno de cultura de "Schizotrypanum cruzi" em soro conservados em geladeira. [Complement Fixation in Chagas's Disease. I. False and Doubtful Positives with Culture Antigen.] *U. sub-Médica.* 1947 Nov. 22 & 29. 61 Nov. 47 48, 398-401 [13 refs.] English summary.

Diagnosis of Chagas's disease in the early stages, when *T. cruzi* is abundant in the blood-stream, is a simple matter; later we have to rely more on xenodiagnosis, inoculation and cultivation. Such methods, especially xenodiagnosis, are lengthy and not always certain. Hence the value of the Guerreiro-Machado reaction in these stages with suspensions of trypanosomes from the blood of infected animals (see this *Bulletin* 1924, v. 3 358 1938, v. 35 771). The authors in this study have used a culture of *T. cruzi* prepared by Davis's method [ibid. 1943, v. 40 880] slightly modified by M. Iz and FREITA (ibid. 1945 v. 41, 875 1947, v. 44 571). They found that sera of some persons, apparently in good health with no signs of infection, gave doubtful and even to some (though not many) cases positive complement fixation if the sera had been kept in an ice-chest even with addition of merthiolate. To avoid this error the reaction must be carried out with fresh obtained serum. The results are shown in protocols.

H. Harold Scott

#### LEISHMANIASIS

HAWKING F. Growth of Protozoa in Tissue Cultures. V. *Leishmaniasis*. *Ann. Roy. Soc. Trop. Med. & Hyg.* 1948 Jan. v. 41 No. 4 545-54. 23 figs. (2 coloured). 15 r. l.

The author has succeeded in cultivating *Leishmaniasis* *donovani* in tissue culture employing hamster spleen as the tissue and rabbit serum as the liquid portion

*Leishmaniasis*

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in place of hamster serum. In cultures made from infected spleens, active multiplication of parasites occurred and these were able to invade uninfected spleen growing in the same Carrell flask. In most of the cultures maintained for more than sixteen days the parasites escaped from the cells and formed masses of flagellates which grew and multiplied at 37°C. Cultures of flagellates growing at 25°C were added to culture of hamster spleen growing at 37°C, some of the flagellates entered cells and appeared as leishmania forms, while other flagellates multiplied in the fluid part of the medium. C M Wenyon

AVERSA, T & CROSCA, A. Modificazioni del quadro ematologico e del mielogramma sotto l'influenza della terapia abbinata di ferro e di antimonio nella leishmaniosi interna infantile [Changes in the Blood Picture and the Myelogram as a Result of Combined Iron and Antimony Treatment in Infantile Kala Azar] *Pediatrics* 1947, v 55, Nos 10/12, 607-21

The English summary appended to the paper is as follows —  
 "The authors have studied the changes of the blood-picture and myelogram under the influence of combined iron- and antimony therapy, in 9 children affected by visceral leishmaniasis

"The improvement of the blood-picture was neither more rapid nor more accentuated than that we generally observe in children treated only with antimony

"Likewise the medullary alterations were not differently modified"

BURGIO, G R. Rilevi statistico-clinici sull'endemia del kala-azar nostrano nella Sicilia occidentale negli anni 1939-1945 [Infantile Kala Azar in Western Sicily] *Pediatrics* 1947, v 55, Nos 1/3, 53-80, 9 graphs & 1 map [30 refs] English summary

Basing his observations on children in Palermo seen at the pediatric clinic, in the children's hospital or attending its out-patient department, the author finds that the cases of kala azar have remained fairly constant, the numbers for 1939 to 1943 being 26, 27, 26, 33, 18. In 1944 and 1945 however, there was a marked increase, the figures 80 and 84 being obtained. This increase was due largely to the cases from the Palermo district. C M Wenyon

CARNEVALE, A. La velocità di diffusione di un elettrolita (HCl), nel gel-serico, nella leishmaniosi interna [Diffusion Speed of an Electrolyte in Frozen Kala Azar Serum] *Pediatrics* 1947, v 55, Nos 1/3, 81-6 English summary (7 lines)

The author has found that an electrolyte (HCl) diffused more rapidly in serum gel of 14 of 15 cases of infantile kala azar (the normal rate being 44-47 mm in 24 hours). This increase to 48-51 mm appears to be related to the alteration which occurs in the albumin/globulin relationship, the globulin being increased in kala azar. In 7 healthy children, a rate of 45 or 46 was obtained. The technique, which consists essentially of gelification of the serum with propionic acid and then adding a layer of HCl and observing penetration of the latter by colour change in Congo red previously incorporated is described. C M. Wenyon

GUIMARÃES, F. N. Visceralização da "Leishmania brasiliensis" Vianna, 1911 em hamsters ("Cricetus auratus") (Nota preliminar) [Visceral *L. brasiliensis* infection in Hamsters (*Cricetus cricetus* = *C. auratus*)] *Brasil-Médico* 1947 Nov. 22 & 29 v. 61 Nos. 47/48 365-6 2 figs. Dec. 29 & 27 Nos. 51/52, 439 (Erratum).

With material taken from a sore containing leishmaniasis, the author inoculated a hamster on the nose and in the peri-ocular region. Seven months later the animal was examined. There were no cutaneous lesions, but there was a generalized leishmaniasis infection which is illustrated by photographs of a section of the spleen and a smear of the bone marrow. This appears to be the first record of a generalized infection with *Leishmania brasiliensis*. Similar infections have been produced by a number of observers with *Leishmania tropica*. In the second note the name of the hamster is corrected to *Cricetus auratus* from *Cricetus cricetus*. C. M. H. Freyre

FULTON, J. D. The Constitution of Photostilbamidine, the Irradiation Product of Stilbamidine. *Brit. J. Pharmacol.* 1948, Mar., v. 3 No. 1 75-9 2 figs. [10 refs.]

"Irradiation of a solution of bases-stilbamidine in sunlight gave a substance which on hydrolysis to the corresponding acid, followed by decarboxylation, yielded a hydrocarbon m.p. 163° identical with that obtained by irradiation of stilbene. The hydrocarbon previously described as di-stilbene has now been shown by x-ray crystallographic analysis to be 1,2,3,4-tetraphenylcyclobutane containing a centre of symmetry. A second isomeric hydrocarbon m.p. 149° was also obtained in the same series of reactions, but its molecular configuration has not yet been determined. The isolation of these two hydrocarbons is in agreement with the view that stilbamidine undergoes dimerization on irradiation of its solutions. [See this Bulletin 1947 v. 44 98d.]

## FEVERS OF THE TYPHUS GROUP

JADIN, J. & D'HOOGER, M. La fièvre rouge congolaise peut être aussi du typhus historique. Cases of Historic Typhus also may be included under the Name Red Fever of the Congo. *Liber Jubilarius J. Huthaus* (See *Belge Méd. T. p. Brussels*) 1947 Dec., 279-90 2 charts. [10 refs.]

Jadin has already isolated strains of murine-typhus rickettsiae from patients regarded as suffering from the red fever of the Congo. See this Bulletin, 1948, v. 45 325.

The authors now claim to have isolated strains of epidemic typhus rickettsiae from three out of eight patients in whose cases the same diagnosis was made.

The features said to be characteristic of the disease are fever, headache, rash, and a West-Petz reaction of the Proteus O/K type.

Six of the eight patients whose cases are described in the present paper reacted with Pr O/K at titres of 1:200 or over; three also reacted with Pr O/A at 1:100 or 1:200 and another with Pr O/A at 1:200.

[There seems to be no valid reason for retaining the name *fièvre rouge congolaise* for fevers shown to belong to the typhus group.]

John W. D. McGee



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*Fevers of the Typhus Group*

GREIFF, D & PINKERTON, H **Effect of Enzyme Inhibitors and Activators on the Multiplication of Typhus Rickettsiae** III Correlation of Effects of PABA and KCN with Oxygen Consumption in Embryonate Eggs *J Exper Med* 1948, Mar 1, v 87, No 3, 175-97, 2 figs [28 refs]

This paper is the third of a series by the same authors [See this *Bulletin*, 1945, v 42, 362, and 1946, v 43, 22]  
Using a special technique, which is described in the paper, the authors found that the rate of uptake of oxygen by eggs containing developing chick embryos became slightly increased on the fourth day after inoculation with rickettsiae and then fell rapidly during the later days

PABA (para-aminobenzoic acid) introduced as described in the earlier papers caused a pronounced increase in the oxygen intake of the infected eggs, whereas MABA (meta-aminobenzoic acid) and OABA (ortho-aminobenzoic acid) caused a moderate degree of depression in the intake

The small doses of potassium cyanide which had been found to enhance rickettsial growth, caused a striking depression in the oxygen intake

These experiments are regarded as supporting the hypothesis that rickettsial growth is inversely proportional to the respiratory rate of the host cells  
Although PABA forms part of the folic-acid molecule, the latter drug in tolerated doses did not increase the oxygen uptake and had no rickettsiostatic action

John W D Megaw

BHATTACHARJYA, B **Clinical Features of Murine Typhus** *Indian Med Gaz* 1947 Sept, v 82, No 9 514-16 4 charts  
A report of seven cases

LANTIN, P T GAMBOA E L & GERONIMO, A **Endemic Typhus with Report of Cases** *Santo Tomas J of Med Manila* 1947 Nov v 2 No 6 293-300  
Describes two cases from Manila

KALRA, S L **Scrub Typhus Variations in Clinical Symptoms and Strains** *Indian Med Gaz* 1947, Sept, v 82, No 9, 516-17

The author presents evidence to show that scrub typhus, even in different parts of the same country, may vary greatly in severity The fatality rates tend to fall into two groups, in one of which they are below 3 per cent while in the other they are 8-10 per cent  
Ty inoculation experiments on the eyes of rabbits, he found that the rickettsial strains from different areas did not always immunize against each other

John W D Megaw

LOEBNER, R J, JELLISON, W L, BECK, M D, PARKER, R R & SHEPARD C C **Q Fever Studies in Southern California I Recovery of Rickettsia burnetii from Raw Milk** *Pub Health Rep Wash* 1948, Feb 13, v 63, No 7, 214-22

The circumstances leading up to the present investigations are stated to have been that studies not yet published had indicated (1) that 117 cases of Q fever had occurred in South California during 1947, (2) that more than half the patients had been workers in dairies or residents in places close to dairies, and (3) that 10-20 per cent of the dairy cows of the Los Angeles area had given positive complement-fixation reactions with Q fever antigen  
The authors give details of the very thorough investigations carried out by them at the U S A National Institute of Health, the Q Fever Laboratory, and

Rocky Mountain Laboratory at all three of which similar results were obtained from the examination of the same samples of milk. Fifty samples of milk were obtained from four dairies, in association with which cases of Q fever had occurred. Most of the samples consisted of pools of milk each of which was obtained from 5-30 cows but a few were from individual cows. Each sample was tested by guinea-pig inoculation, and from 40 of them evidence of Q fever infection was obtained in the form of complement fixation reactions against Q fever antigens. Most of the reacting guinea-pigs had febrile reactions, and from eight of these, which were sacrificed, strains of *Rickettsia burnetii* were isolated by further guinea-pig inoculation and by yolk-sac culture.

Each of several strains that were tested for cross immunity against known strains of *R. burnetii* gave positive results.

None of the infected cows showed any signs of illness or of diminution in the yield of milk. The available evidence did not suggest that infection was transmitted to human beings by drinking milk, though it was considered possible that milk might be a source of infection by some mode yet to be determined.

John W. D. Meyer

## YELLOW FEVER

WADDELL, Mary B. & TAYLOR, R. M. Studies on Cyclical Passage of Yellow Fever Virus in South American Mammals and Mosquitoes. IV. Marsupials (*Metachirus nudicaudatus* and *Marmosa*) in combination with *Aedes aegypti* as Vector. *Amer J Trop Med.* 1948, Jan., v 28, No. 1 87-100 3 figs. [14 refs.]

The authors have found that under appropriate conditions in the laboratory certain strains of jungle yellow fever virus may be maintained in cyclical passages through marsupials (*Metachirus nudicaudatus* and *Marmosa*) in combination with *Aedes aegypti* as the insect vector and that strain differences of the virus may be of such magnitude as to affect their cyclical passage in *Metachirus*. These strain differences, at least in so far as the host vector cycles are concerned, are influenced by the nature of the host and possibly of the vector through which recent passages have occurred.

These marsupials, when they are infected, do not so readily, or so consistently infect normal mosquitoes as do two species of marmosets which have been studied.

The results of these laboratory experiments suggest that *Metachirus nudicaudatus* and *Marmosa* can, under favourable circumstances, serve as vertebrate hosts in the maintenance of certain strains of jungle yellow fever but before they are incriminated as natural hosts of the virus, supporting epidemiological evidence is required. In a rather comprehensive field study in a region where the disease is endemic in the forests, no information was obtained which implied that marsupials played a significant role in the propagation of the virus [see this Bulletin 1947 44-414].

F. O. MacCallum

HUGHES, T. P. & PERLOWAGORA, Alma. The Reaction of certain Species of Bats to Yellow Fever Virus. *Amer J Trop Med.* 1948, Jan v 28, No. 1 101-5

The possibility that yellow fever virus may be disseminated between isolated forest patches through transport by flying vertebrates has been suggested frequently but has been subjected to little experimental test. Hughes (see this Bulletin, 1933, v 30 6) failed to find virus in the blood streams of bats bitten by

*Aedes aegypti* infected with either of two strains of yellow fever virus More recently, LAENMERT *et al* [see this *Bulletin*, 1947, v 44, 414] found that only one of 81 bat sera from an area of endemic yellow fever infection neutralized the virus, and they considered this one result non-specific

Hughes and Perlowagora carried out a total of 254 tests for the presence of virus in the sera of bats which had been exposed to it, either by injection or by mosquito bite, but no virus was detected Neither did any of the 55 bats which were tested develop neutralizing antibodies as a result of this exposure They used *Eumops californicus*, *Phyllostomus panamensis* and *Molossus* sp which frequent forest areas

These results indicate that tests on sera of captured wild bats can give no information as to whether these vertebrates have previously been in contact with yellow fever virus

F O MacCallum

FOX, J P, DA CUNHA, J F & KOSSOBUDZKI, S L Additional Observations on the Duration of Humoral Immunity following Vaccination with the 17D Strain of Yellow Fever Virus *Amer J Hyg* 1948, Jan, v 47, No 1, 64-70

This is a report of examination of sera of several vaccinated groups in whom immunity has been followed for several years

Though there has been some diminution in the percentage of individuals with strong protection in the mouse protection test, 4 to 6 years after inoculation practically all sera still contained detectable antibody As in a previous study by FOX & CABRAL [this *Bulletin*, 1943, v 40, 451], there was a suggestion of short duration of immunity in children, but the difference between results in children and older persons was not statistically significant,

These results, together with those of SMITHBURN and MAHAFFY in Uganda [see this *Bulletin*, 1946, v 43, 34] and BUGHER and GAST-GALVIS in Colombia [*ibid*, 1944, v 41, 478] give complete support for the four-year certificate of immunity to yellow fever which is in current use

F O MacCallum

FRORS H P Proyecto de campaña continental para la erradicación del *Aedes aegypti* [Scheme for a Pan-American Campaign towards the Eradication of *Aedes aegypti*] *Bol Oficina Sanitaria Panamericana* 1947 Oct v 26, No 10 842-51 English summary

See also p 485, GIGLIOLI, An Investigation of the House-frequenting Habits of Mosquitoes of the British Guiana Coastland in relation to the Use of DDT

DE CAIRES, P F *Aedes aegypti* Control in the absence of a Piped Potable Water Supply *Amer J Trop Med* 1947, Nov, v 27, No 6, 733-43, 12 figs

The classical *Aedes aegypti* control measures, as established in Brazil by the International Health Division of the Rockefeller Foundation, were employed in British Guiana during the recent war years, the Colony having a vitally important source of supply of bauxite Briefly, these measures amounted to a system of careful inspection of waters for larvae of *Aedes aegypti*, this involved the provision of staff for inspection of water containers in and around dwellings, in dock-areas and shipping, and of water collections difficult of access, lastly other persons were trained for adult mosquito catching *Aedes aegypti* house indices (the percentage of houses inspected in which adult mosquitoes or water receptacles containing pupae, larvae or eggs were found) became low, but fluctuated with rainfall, and eradication was not achieved in urban areas Persistence of breeding was contributed to by a 4-day egg-to-adult cycle which occurred at times it was not practical nor economical to increase the inspection rate from a 7-day to a 4-day interval

Georgetown (8° N 58° W) with a population of 80,000 has no piped potable water supply and in consequence rainwater is collected from the roofs by galvanized roof gutters and the water is led into large storage containers such as vats, tanks, barrels and drums. The variety of breeding places, and the methods of inspection and control, are adequately described and illustrated. The necessity for strict discipline of inspection squads is stressed, the process of constant checking of the work of inspectors, of discovering their inefficiencies, and bringing them to book, is unpleasant but essential.

The human factor of inefficiency in inspection is eliminated by the introduction of DDT applied on one occasion as a residual insecticide to the interior walls of all houses. Hidden foci of breeding are no longer a source of trouble. A five per cent. solution of DDT in kerosene is applied at an estimated dosage of 100 mgm. DDT per square foot of wall and ceiling. The cost for a 3 to 5-roomed house is about £ 8 dollars which represents 0.47 to 0.59 dollars (British West Indies) per head of population. The overall cost is much cheaper than the cost of the classical inspection service. In rural areas, the classical method could produce a zero index in four months at a cost of 1.30 dollars per head of population, urban costs being infinitely greater.

The Georgetown *Aedes aegypti* house index, which under classical control methods fluctuated between 1 and 3 per cent, fell to zero within 12 months of the introduction of the use of DDT as a residual insecticide. In the event of *Aedes* re-establishing breeding in an area, it is believed that a single localized re-application of DDT will be effective in eradicating the focus within a few weeks.

R. Ford Travis

## DENGUE AND ALLIED FEVERS

FLORIO L. & MILLER, Mabel S. Epidemiology of Colorado Tick Fever (cont.)  
*Pub. Health* 1948, Feb., v 38 No. 2, 711-13.

The presence of the virus of Colorado tick fever was demonstrated by hamster inoculation in nine out of ten pools of ticks (*Dermacentor andersoni*) collected from areas in Denver where the disease is endemic.

In a study of experimental infection among ticks it was found that hamsters could be infected by the bites of larvae whose parents had been infected by biting infected hamsters. By inoculation experiments it was shown that larvae, nymphs and adults belonging to the same brood of infected ticks were infective to hamsters, though the eggs of these broods were not infective.

Larval ticks fed on infected hamsters remained infective after reaching the nymphal and adult stages.

Dog ticks (*Dermacentor variabilis*) collected in Long Island, where the disease is not known to occur, were found to be infected with a virus similar to, or identical with, the virus of Colorado tick fever.

John H. D. MacLeod

## PLAGUE

TIEN T. H., LANDAUER E., MIYAGI W. F., KOBAYASHI, G. & OKADA Y. G.  
 Primary Pneumonic Plague in Mukden, 1946, and Report of 29 Cases. 24  
 3 Recoveries. *J. Jap. Dis.* 1948 Jan Feb 62, No. 1 52-8 3 figs.  
 (20 refs.)

Primary pneumonic plague in Manchuria is not a new occurrence for there were the epidemics of 1910 and 1920. What is new for this very fatal and

## Plague

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infective type of plague is the report of three recoveries. Although these cases occurred towards the end of the epidemic the circumstances point to the use of sulphadiazine as "the principal factor in the recovery" of three out of five patients treated. The authors believe that the infection was started by a carrier who came into Mukden during the incubation period and died after a very short illness. Contacts of proven cases of primary plague were quarantined, they numbered 67, and 23 of these developed plague. An interesting point is emphasized that, out of 42 individuals without symptoms, who had throat swabbings made daily, 4 were found to harbour virulent *P. pestis* and that this infection persisted for 6 to 15 days. "At least one of the 4 is believed to have been a true healthy carrier".

W F Harvey

PUBLIC HEALTH REP Wash 1948, Feb 20, v 63, No 8, 243 Plague  
Infection in Dawson County, Texas

As a result of evidence of plague in native rodents in Cochran County and in Dawson County, Texas in 1946 and 1947, respectively, the Texas State Dept of Health, in co-operation with the U S Public Health Service, surveyed the ecology of the reservoirs and vectors of plague in the affected counties.

At the end of 1947 it was reported, as a result of these studies, that plague infection had been found again in Dawson County, eight miles west of Lamesa. The infection was detected in a pool of 141 fleas from 14 pack rats (*Neotoma micropus*).

H J O'D Burke-Gaffney

ARAÚJO COSTA, Gobert Contribuição ao diagnóstico da peste nos ratos.  
[Diagnosis of Plague in Rats] Monografias do Serviço Nacional de Peste I  
Rio de Janeiro, Brasil 250 pp [Bibliography]

A monograph of 250 pages restricted to the diagnosis of plague in rats might be doubtfully regarded as a real work of reference. It may be stated, therefore, at the outset that the abundant information contained in it, after a full historical introduction of 50 pages, relates as much to bacteriology as to zoology. A full summary indicates how much is the author's own personal experience. From the examination of 10,000 rats, by which only two were found to be infected with plague, in Rio de Janeiro, and how much is a penetrating analysis and test of claims made by other authors. A short set of conclusions is, itself, a summary, and the bibliography extends to 334 references, each of which is presented under full explanatory title. There are no illustrations and no graphs, but there are many full tables which are in many respects more useful than graphic presentations. We have now for some time been accustomed to very thorough deliverances on plague from America and owe a great deal of our knowledge of epizootic and enzootic plague to these. One might even, protestingly and without seriousness, speak of America as the "home" of plague, a mere counterblast to the description of India as the "home" of cholera. The fact that this work is written in Portuguese should not be a deterrent to its use by anyone who is well versed in the subject matter, for it is easy to read and is packed with information.

Some of the facts, or, as the case may be, conclusions, can be shortly set out — The rats reached the laboratory in a varied condition, some 1,500 still alive, some recently dead and many in an advanced state of decomposition. Necropsies were undertaken in those of the species *R. norvegicus*, *R. r. alexandrinus*, *R. r. rattus* and *M. musculus*. Fleas on these rodents belonged in greatest number, 593 out of 598, to the species *X. brasiliensis* and *X. cheopis*. Special attention was paid to the possibility of organismal non-plague infections, contaminating and epizootic, which can lead the field worker astray in the

diagnosis of plague. Even *Trypanosoma lewisi* came in for attention, as might diseases like tularemia and melioidosis. Contaminating organisms of sub-aerogenes, *Proteus* and *Salmonella* groups often give trouble morphologically. It is evident that the author separates the pasteurillas of the animal haemorrhagic septicaemias, which seem to be one for every animal (or a toxic unit *canis lupus caninus gallinae* etc.) from *Pasteurella pestis*. The chief differentiation, however that is obligatory in the rat is that of *P. pestis* from *P. pseudotuberculosis rodentium* and this receives full consideration.

Four methods are singled out for a presumptive test and these are designated, the classical method, the method of thermoprecipitation that of bone marrow puncture and the flea examination. Full identification is supplementary to the presumptive test. The author maintains strongly the value of bone marrow examination in decomposed animals. A great many suggested culture media have been examined for their selective differentiation value and the characters of the plague bacillus which are stressed are morphology motility at 22°C (Levinthal's method) fermentation of glucose lactose and saccharose the indole methyl red and reductase tests and finally an inoculation that is to say guinea pig test. Much valuable direction is given to the type of plague, acute and chronic, especially in the declining episode which may justly bear such names as mitigated benign, resolving, residual and inapparent plague.

An index would add greatly to the value of this monograph as a reference work.

[It is rather surprising that in a great many extensive bibliographies, as this one is, there should be no reference to the Royal Indian Commission (1906-09) although we find references to German, Austrian, English and even Astrakhan Commissions. In historical texts and in text books, too the "Existence of an Endemic Focus of Plague in the Foothills of the Himalayas" is very little noticed although it was given a chapter in the Commission Report referred to, and by HAXKIN (*Ann. Inst. Pasteur* 1898, v 12, 711). It existed before the arrival of plague at Bombay from Hong Kong and was said to be commonly preceded by a rat epizootic. Another constant omission which is understandable considering the local character of the publications, is reference to the basic investigations of Glen Liston on rat flea transmission of plague and to Ashburnton Thomson's Report on the Second Outbreak of Plague in Sydney 1902. They formed very important supplements to the work of Semond in Bombay and were milestones on our path of knowledge. Liston's first study of "Plague Rats and Fleas" and the part the latter played in the transfer of plague from rats to man was communicated to the Bombay Medical and Physical Society in February 1903 and a second to the Bombay Natural History Society in April 1903.]

W. F. Harry

## CHOLERA

SMITH W. E. & PIERCE R. B. Reducing the Pyrogenicity of Concentrated Protein Solutions. *J. Bacteriol.* 1947 Dec 54 No. 4 715-18.

The pyrogenicity of concentrated protein solutions can often be reduced by treatment with decalco and by filtration through 5-6 pads of the Republic series.

"The amount of decalco and the area of pad space used are functions of the degree of pyrogenicity and of the protein concentration of the solution, and for maximum effect, none they should be determined for each solution to be

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PASRICHA, C L, PAUL, B M, DAS GUPTA, A C & DAS, A K Sulphadiazine in the Treatment of Cholera. *Indian Med Gaz* 1947, Sept, v 82, No 9, 518

"A series of 425 cholera patients were treated with sulphadiazine in addition to the usual saline supportive treatment The death rate in this series was 8.2 per cent A parallel series of 423 control cases not treated with sulphadiazine gave a death rate of 9.5 per cent

"Another series of 451 cases treated with sulphadiazine was compared with a parallel series of 463 cases treated with sulphaguanidine The mortality in the sulphadiazine series was 7.9 per cent whereas in the sulphaguanidine series it was 4.3 per cent

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PASRICHA, C L, PAUL, B M, DAS GUPTA, A C & DAS, A K Sulphaguanidine in the Treatment of Cholera *Indian Med Gaz* 1947, Sept, v 82, No 9, 518-20

"A series of 1,118 hospitalized cholera patients were treated with sulphaguanidine with a death rate of 3.7 per cent A parallel series of 1,170 control cases were treated in exactly the same way but not given sulphaguanidine and the death rate was 7.5 per cent A series of 60 cholera patients were treated with sulphaguanidine in village homes No supportive treatment was possible The death rate in this series was 18.3 per cent, whereas in a parallel control series of 59 cases, the death rate was 40.7 per cent

"Sulphaguanidine is thus of considerable value in the treatment of cholera"

SEAL, S C Sulphaguanidine in the Treatment of Cholera under Rural Conditions. (A Report on 290 Cases) *J Indian Med Ass* 1947, Dec, v 17, No 3, 85-90

Many reports now bear witness to the value of sulphaguanidine in the treatment of cholera in hospital patients Such patients are generally late arrivals and the treatment might be more effective still at an earlier stage of the disease The present account relates to 30 small outbreaks of cholera in 29 villages, where the treatment was carried out under actual field conditions in which both the community and the environment remained uncontrolled The total number of cases was 290, and sulphaguanidine was used in 134, with only two deaths the remainder, not alternate cases but treated otherwise, furnished 67 deaths The difference in the fatality rates is very significant, the proportion of 1.5 to 43.5 per cent, respectively No toxic symptoms could be ascribed to the sulphaguanidine, which was administered as initial dose of 3 gm followed by further doses of 3 gm every 3 hours, until stools were reduced in number to two or less per day, after which the dose became 1 gramme every 6 hours for the next 24 hours The author considers that the drug may be safely kept in villages and administered generally in suspicious gastro-intestinal diseases as an emergency or first aid measure

W F Hurst

diagnosis of plague. Even *Trypanosoma lewisi* came in for attention, as do diseases like tularaemia and melioidosis. Contaminating organisms of the aerogenes, *Proteus* and *Salmonella* groups often give trouble morphologically. It is evident that the author separates the pasteurellas of the animal haemorrhagic septicaemias, which seem to be one for every animal (or at least *canis caprea caniculi gallinae* etc.) from *Pasteurella pestis*. The chief demerit, however, that is obligatory in the rat is that of *P. pestis* from *P. pseudotuberculosis rodentium* and this receives full consideration.

Four methods are singled out for a presumptive test and these are designated, the classical method, the method of thermoprecipitation, that of bone marrow puncture and the flea examination. Full identification is supplementary to the presumptive test. The author maintains strongly the value of bone marrow examination in decomposed animals. A great many suggested culture media have been examined for their selective differentiation value and the characters of the plague bacillus which are stressed are morphology, motility at 22°C. (Levinthal's method), fermentation of glucose lactose and saccharose, the indole methyl red and reductase tests and finally an inoculation that is to say guinea pig test. Much valuable direction is given to the type of plague, acute and chronic, especially in the declining epizootic which may justly bear such names as mitigated, benign, resolving, residual and inapparent plague.

An index would add greatly to the value of this monograph as a reference work.

[It is rather surprising that in a great many extensive bibliographies, as this one is, there should be no reference to the Royal Indian Commission (1894-97) although we find references to German, Austrian, English and even Australian Commissions. In historical texts and in text books, too, the existence of an Endemic Focus of Plague in the Foothills of the Himalayas is very little noticed although it was given a chapter in the Commission Report referred to, and by HAXELL (*Ann. Inst. Pasteur* 1898, v. 12, 711). It existed before the arrival of plague at Bombay from Hong Kong and was said to be commonly preceded by a rat epizootic. Another constant omission, which is understandable considering the local character of the publications, is reference to the basic investigations of Glen Liston on rat flea transmission of plague and to Abbington Thomson's Report on the Second Outbreak of Plague in Sydney 1902. They formed very important supplements to the work of Semcoz in Bombay and were milestones on our path of knowledge. Liston's first study of 'Plague Rats and Fleas' and the part the latter played in the transfer of plague from rats to man was communicated to the Bombay Medical and Physical Society in February 1903 and a second to the Bombay Natural History Society in April 1903.]

15 F. HARRIS

## CHOLERA

SMITH W. E. & PENNELL R. B. Reducing the Pyrogenicity of Concentrated Protein Solutions. *J. Bacteriology* 1947 Dec. 54 No. 4, 715-18.

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W F Harvey

LORESTANO H J & BARTER, M. E. Investigation of some Newer Sulfonamides as Intestinal Chemotherapeutic Agents. *J Pharm. & Exper Therap* 1948, Feb. v 92 No. 2, 193-208, 1 fig [23 refs.]

"Preliminary study of three new sulfonamides as intestinal chemotherapeutic agents is reported: 2-sulfanilamido-5-carbamylthiazole (N-succinamylsulfanilamido) thiazole and 2 (N-succinylsulfanilamido) 1,3,4-thiadiazole

"The presence of the carbamyl group in the 5-position of sulfathiazole greatly reduces absorption from the gastro-intestinal tract and activity *in vitro*. However marked anti-coli action was demonstrated in mice and dogs. Sulfacarbamylthiazole is relatively stable and activity is apparently due to the drug *per se*.

"Replacement of the carboxy group of succinylsulfathiazole with the carbamyl group yields a compound considerably more labile than the parent drug. While absorption was slight following oral administration of succinamylsulfathiazole to mice and dogs, the drug showed but little anti-coli activity *in vivo*.

"Substitution of the succinyl radical in the N<sup>1</sup> position of sulfathiazole results in a compound highly active in the intestinal tract of both mice and dogs and only slightly absorbed into the blood. The anti-coli activity of succinylsulfathiazole was found to be much greater than that of sulfathiazine in mice and about equal to the latter drug in dogs. Data seem to establish succinylsulfathiazole as a potentially useful drug for trial in therapy of enteric infections.

BRATNAGAR, S S FERNANDES, F DE SA, J & DIVKAR, P V. A New Sulpha Compound ("6257") and its Use in Human Cholera Infection. (Communication). *Nature* 1948, Mar 13, 385-8.

Sulphonamides have become currently used drugs in cholera. A new compound is now put forward with considerable promise of cure. It is described as a condensation product of two molecules of 2 p-amino-benzene sulphonamido-thiazole (Cibazol) and three molecules of formaldehyde with molecular weight much greater than that of any other sulpha compound so far employed in clinical therapy.

*In vitro* experiments have shown this substance to have bacteriostatic power and, in greater concentration, powerful bactericidal action. Further experimentation *in vivo* on mice gave indication that pre-infectious administration by subcutaneous or intraperitoneal routes could protect mice against intraperitoneal injection of 2 MLD of cholera toxin. The drug has already been tried in the field in total dosage of 23 gm. given as 10 gm. on the first day, two doses of 4 gm. on the second day and two 1 gm. each morning and evening every subsequent day for five days. Some 83 cases of bacteriologically established cholera have undergone treatment and the mortality was only 4 per cent, presenting a marked contrast to the estimated mortality of more than 60 per cent during the past season. It is important to note that no toxic effect even with a maximum dose of 50 gm. were observed. The drug may also be used prophylactically. W F Harry

## AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

STARKEY, H & POOLE, J Survey of Intestinal Parasites in Repatriated Prisoners of War from Hong Kong *Canadian Med Ass J* 1947, Oct, v 57, No 4, 377-9

The authors examined the stools of 453 Canadian ex-prisoners of war from Hong Kong several months after their repatriation to Quebec and the Maritime Provinces. Normal stools were examined daily for 3 days and again on the 5th and 6th days. On the 4th day a fresh specimen was examined after purgation. Direct examination for parasites was made in saline and identification was based on stained preparation. Washed stools were examined for cysts by the standard zinc sulphate flotation method.

In 231 cases parasites were found in normal stools and in 41 they were only found after purgation. In many cases they were found in the specimens of the 5th and 6th days and not in the purge specimen itself. Pathogenic parasites were found in 26.7 per cent of cases and non-pathogenic in 41.3 per cent. Of the former, *Giardia* and *Ascaris* accounted for some 9 per cent each, *E. histolytica* for 7 per cent and *Ancylostoma* for 4 per cent. (It is pointed out that these percentages are individual, owing to the presence of mixed infections in some cases.)

*E. coli* was found in 36.4 per cent, *Endohmax nana* in 22.5 and *Trichuris trichiura* in 17 per cent.

Other parasites were found in less than 3 per cent of patients. The findings are analysed in relation to a history of amoebic dysentery, of intestinal upsets, of general asthenia and of no complaints since return to Canada.

From this analysis, it is revealed that *E. histolytica* occurred in 3.6 per cent of those without histories or symptoms of acute amoebic dysentery, of those returning to Canada, in 7.5 per cent of those with a definite history, and in 9.5 per cent of those with vague symptoms.

It is pointed out that the group under survey had been examined, and where necessary treated, on their arrival in Canada. The authors refer to the findings of MILLER (*Canadian Med Ass J* 1946, v 55, 336) who suggested that the incidence of *E. histolytica* in the general population of Canada was probably about 2 per cent. In the present survey it was about 7 per cent. The only sub-group in this survey approximating to the incidence quoted for the general population was that of men having no history of typical amoebic dysentery and no complaints since returning to Canada (3.6 per cent).

The authors conclude that in routine survey of faeces for parasites, it is desirable to include a purge in the routine, and also to examine more specimens for at least two days thereafter. They also conclude that those who were prisoners of war in the Far East carry a higher percentage of pathogenic intestinal parasites than do residents of Canada.

H J O'D Burke-Gaffney

ANDERSON, H H & HANSEN, E L Cultivation of *Endameba histolytica* Libr *Jubilaris J Rodhain* (Soc Belge Méd Trop, Brussels) 1947, Dec, 47-61, 2 figs [43 refs]

The authors trace the development of media for the cultivation of *E. histolytica* since BOECK and DRBHOLAY's success in 1925. They finally describe a new medium containing only synthetic products. There are 12 amino-acids, nucleic acid, rice powder, cholesterol, 11 vitamins and various salts. In it, with only a single bacillus "t", over 170 compounds have been tested for their

amoebicidal activity. Contrary to expectation, based on LAIDLAW's findings with emetine various agents were not uniformly more active in the liquid medium. The activity of the arsenoxides was lower in the liquid medium than in that with a solid base. With most other chemical types only insignificant differences were noted. It is hoped that a medium containing only synthetic ingredients may afford an understanding of the growth requirements of *E. histolytica*.

C. M. HENSON

DOBELL, C. An Improved Method for testing the Action of Emetine and other Chemicals on *Entamoeba histolytica* in Cultures. *Liber Jubbiana / Rotham* (Soc. Belg. Méd. Trop. Brussels). 1947 Dec., 201-11 (15 refs.)

By the use of a liquid medium consisting of dilute horse-serum (1-8 Ringers fluid) with rice starch and 0.2 per cent. disodium hydrogen phosphate as buffer cultures of *E. histolytica* have been obtained and used for testing the action of emetine. This medium, first described by LAIDLAW, DOBELL and BILSON in 1928, has been employed by Dobell since then. The amoebic culture has been purified so that *E. histolytica* with the single organism *Bact. coli* have been obtained. In order to ensure that the amoebae grow in subculture the medium is inoculated with the bacillus and incubated for 24 hours before the amoebic subculture is made into it. In this way it has been shown that emetine in a strength of 1-5,000,000 is invariably fatal to *E. histolytica* within 4 days and that they sometimes succumb to dilutions of 1-20,000,000. The author thinks that by following the technique described in the paper there is an opportunity of testing the action of other substances which are calculated to cure amoebic dysentery.

C. M. HENSON

SIGUET, F. SARRATIN, A. & PÉRIER, R. Typhlo-hépatite amébienne récurrente à court terme évoluant depuis deux ans chez une coloniale transplantée. [Amoebic Typhlo-Hepatitis with Frequent Relapses at Short Intervals during Two Years.] *Bull. et Mém. Soc. Méd. Hôp. de Paris*. 1948, Vol. 1/2, 27-30.

The authors describe a condition they refer to as an amoebic typhlo-hepatitis with frequent relapses at short intervals. The symptoms and signs are incoercible  $\pi$  but there is infiltration of the caeco-colic region in association with hepatic pain and discomfort and prostration. This liver trouble recurs at short intervals - in some cases it resolves spontaneously in others it responds to emetine, and in yet others it is resistant to emetine.

They describe in detail such a case of suspected liver involvement without any evidence of frank abscess - this was treated for over two years on each recurrence with emetine with temporary benefit. The patient in due course showed evidence of emetine poisoning and she finally abandoned. 1 R. D. Adams

ACLESAN, H. J. F. & GARDNER, H. Hepatic Amebiasis. *U.S. Vet. Med. Bull.* 1948, Jan. Feb. v. 48 No. 1 22-39 10 figs. 14 refs.

In the sense of this paper the term hepatic amoebiasis covers amoebic hepatitis and amoebic abscess of the liver. The three possible routes of invasion by the amoebae are discussed. (1) Direct extension through the bowel wall, peritoneal cavity and capsule of the liver. (2) Extension by the lymphatic route. (3) Extension from the bowel through tributaries of the portal vein, generally considered to be the most common method.

Hepatic amoebiasis is suggested in cases which fail to respond to penicillin therapy with or without sulphonamide and which present signs pointing to

acute liver disease, with or without jaundice, and accompanied by leucocytosis, chills and fever. The elimination of intestinal amoebic infection forms an important part in the treatment of hepatic amoebiasis. In the six cases detailed in this report, open operation and aspiration were avoided. This is ascribed to early recognition and intensive treatment with emetine injections and diodoquin where secondary infection is present (and it is suggested that 50 per cent of amoebic abscesses of the liver are so infected at the time of diagnosis) penicillin and emetine would appear to be a wise combination. One case with constant lumbar pain is described which suggested formation of an amoebic perinephric abscess. The pain and fever were relieved by emetine injections. The method of pneumoperitoneum is employed as a means of delimitating the lower edge of the liver. Penicillin therapy alone is regarded as of no value, but should be considered a valuable adjunct to emetine when secondary invading organisms are suspected. *P Manson-Bahr*

HAYS, T G, BROWN, R B & GODFREY, E W **Liver Abscess** *U S Nav Med Bull* 1948, Jan-Feb, v 48, No 1, 7-21, 5 figs

During five months from December 1945 to May 1946, 10 cases of liver abscess were treated in a U S Naval Hospital. Several of them illustrate many important points in diagnosis and treatment. The clinical picture may be anything but characteristic. The pain in the right lobe of the liver is usually dull and intensified by deep pressure.

Laboratory studies may be of limited diagnostic value, and liver function tests, even the icterus index, and the van den Bergh reaction, are not uniformly or significantly altered. The most reliable aid to diagnosis is provided by radiography. Elevation of the right dome of the diaphragm is purely mechanical, restriction of movement is primarily irritative and increases with proximity of the abscess to the dome. Areas of atelectasis or pneumonitis within the lung tissue, or fluid in the pleural sulcus, are secondary to the inflammatory process below the diaphragm. Serial films, showing increasing size of the liver, or progressive elevation of the dome of the diaphragm, are of particular significance.

The cases here recorded were treated by open surgical drainage, but it is admitted that some of the patients might have been cured on a more conservative régime. Seven of the ten cases were correctly diagnosed before operation. Two were operated as cases of acute cholecystitis and in one the true diagnosis was revealed post-mortem.

Three in whom amoebiasis was suspected as the chief aetiological factor returned with further complications attributable to this infection. Initial prompt but incomplete, therapeutic response to penicillin on two occasions in one case, suggested a superimposed bacterial infection, though this was not confirmed at operation and by culture. It is suggested that more intensive treatment of the underlying amoebiasis with emetine and carbarsone might have prevented recurrences. *P Manson-Bahr*

MANSON-BAHR, P **Secondary Bacterial Infections of Amoebic Abscess of the Liver** *Liber Jubilaris J Rodhain (Soc Belge Méd Trop, Brussels)* 1947, Dec, 291-301, 5 figs [13 refs]

In the diagnosis and treatment of amoebic liver abscess, the possibility of secondary bacterial infection must always be considered. In abscesses of old standing, such contamination is not uncommon. The implications of its existence are insufficiently appreciated. Early cases of hepatic amoebiasis

respond well to emetine. Later cases may fail to do so owing to bacterial infection and repeated aspiration fails to relieve these. After surgical drainage such cases recover.

There is little reference in the literature of the last 35 years to proven secondary infection of amoebic liver abscesses, and none as to the route of infection, but it does occur. In 60 of the author's cases of amoebic liver abscess, 41 were found to be bacterially infected. In only four of these could active amoebae be found in the aspirated abscess contents. *E. histolytica* cysts were recovered from the stools of 45 per cent. of patients with amoebic liver abscesses.

The author envisages the development of an amoebic liver abscess as follows. There is a massive portal invasion of the liver with amoebae producing an allergic response with engorgement and swelling of the organ to about twice its normal size. Large numbers of amoebae are distributed throughout the liver lobules but the majority are destroyed. A few survive and multiply as a focal point causing a single abscess which initially resembles a gumma or a tuberculous nodule rather than an abscess. In this solid stage the amoebae multiply at the periphery and are not found in the centre. The centre of the lesion liquefies by cytolytic action; the liquefaction extends radially and the contents of the cavity become a sterile fluid pus. In some rare cases this becomes inspissated, and absorbed or calcified. The author has seen four calcified abscesses one of over 20 years' duration without the patient's having been aware of its presence. Aspiration of the pus before liquefaction takes place is impossible but emetine injections kill the amoebae and the material is absorbed. After liquefaction has taken place emetine is not effective unless the pus is drained. If this pus is bacterially infected aspiration is inadequate and emetine therapy is ineffective. Surgical drainage is necessary.

The routes by which bacterial infection of the liver parenchyma may occur are—(1) by rupture of the abscess through the diaphragm and direct infection via the respiratory tract; this is probably the most common; (2) by direct absorption from the large intestine possibly by extension from the hepatic flexure of the colon in close proximity to the liver by *Bact. coli* and other intestinal organisms; (3) as part of a general septicaemia from a septic focus such as a boil on the surface of the body.

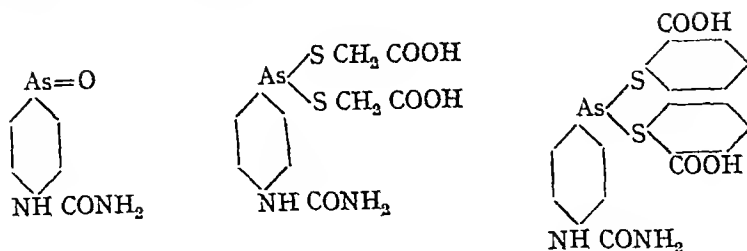
Five cases of amoebic liver abscess secondarily invaded by bacteria are cited to illustrate these modes of bacterial infection. The invading organisms identified were *Bact. coli* and a long-chain *Streptococcus Streptococcus viridans*, *Staph. aureus* and *Staphylococcus aureus*. In conclusion, the author contends that it is better to regard an amoebic liver abscess as bacterially infected until proven otherwise. Alteration in the temperature chart from an intermittent to a high remittent type is indicative of this secondary infection.

J. R. D. Jones

COLE, A. I. & ACHUTON. A Case of Amoeboma with Abscess Formation Followed by Infection of the Drainage Wound. *India M J Gaz.* 1947 Sept., 82, No. 9, 339-41.

ANDERSON, H. H., HANSEN, E. L., NAM, P. P. T. & CASIN, J. R. Amoebicidal and Pharmacologic Activities of Carbarosone Oxide (P-Carbamidophenyl-arsenous Oxide) and its Dithiocarboxymethyl and Dithiocarboxyphenyl Derivatives. *J. Pharm. & Exp. Ther.* 1947 Oct., 91, No. 2, 112-23, 11 refs.

Carbarosone has been used extensively in the treatment of amoebiasis. The corresponding carbarosone oxide and the dithio derivatives named in the title have the following formulae—



The amoebicidal action of these four substances and of emetine have been compared *in vivo* and *in vitro* by the methods previously described by the authors [this *Bulletin* 1947, v 44, 819]. Before clinical trials on monkeys naturally infected with *E. histolytica*, toxicity tests were carried out on the white cells of rabbits and on various laboratory animals. The pathological effects produced were studied in some detail. In the monkey, carbarsone oxide and the above derivatives were found more active than the pentavalent carbarsone, while emetine in effective doses was not well tolerated. Details are given of the methods employed in studying the distribution of arsenic in tissues after administration of arsenicals by different routes. Carbarsone oxide gave rise to high levels of arsenic in bile, blood and urine, and smaller amounts were present in other tissues. The distribution of arsenic after dithio derivatives was somewhat different and levels were not so high. The level remained appreciable for some days after administration. The amount bound by tissues was roughly paralleled by toxicity. Fewer pathological changes were produced by the dithio derivatives than by the parent oxide. The introduction of these groupings did not, however, appreciably affect amoebicidal activity *in vitro* or *in vivo*.

J. D. Fulton

GOODWIN, L G, HOARE, C A & SHARP, T M The Chemotherapy of Amoebiasis Part I Introduction and Methods of Biological Assay *Brit J Pharmacol* 1948, Mar, v 3, No 1, 44-8 [22 refs]

GOODSON, J A, GOODWIN, L G, GORVIN, J H, GOSS, M D, KIRBY, K S,  
LOCK, J A, NEAL, R A, SHARP, T M & SOLOMON, W The Chemo-  
therapy of Amoebiasis Part II Amines derived formally from Emetine  
*Ibid* 49-61

\_\_\_\_\_, \_\_\_\_\_, \_\_\_\_\_, \_\_\_\_\_, \_\_\_\_\_, \_\_\_\_\_, \_\_\_\_\_, \_\_\_\_\_, \_\_\_\_\_ & \_\_\_\_\_ The Chemotherapy of  
Amoebiasis Part III Variants of Bis(diamylamino)decane *Ibid* 62-71  
[13 refs]

I In this series of papers is described a systematic search for new amoebicides whose structure has been based on that of emetine and of certain compounds found by PYMAN (*Rep Brit Ass* 1937, v 107, 60) to be active *in vitro*. Methods for comparing the activity of these substances *in vitro* and *in vivo* are described. For the former tests, a culture of *E. histolytica* grown with a single bacterium (*Bact coli*) was maintained in culture on the horse-serum-Ringer-egg medium of DOBELL & LAIDLAW [this *Bulletin*, 1927, v 24, 363]. In the actual test the buffered horse-serum Ringer medium of LAIDLAW *et al* [this *Bulletin*, 1929, v 26, 469] was used to which the appropriate concentration of drug in sterile buffered Ringer solution was added and then a heavy inoculum of *Bact coli* and a small quantity of sterile rice starch. After incubation at 37°C overnight, the bleaching of an added drop of dilute methylene blue solution indicated that conditions in the medium were satisfactory for the growth of amoebae. A heavy suspension of *E. histolytica* from the stock cultures was then added to each tube by pipette. After incubation for 3 days, the contents of the tubes were

examined microscopically for the growth of amoebae the pH of the ulcers was checked and the viability of the bacteria tested by subcultures. The 1510 tests in which young rats of weight 20 to 30 gm. were used immediately after weaning were carried out in a manner similar to that described by JONES (this Bulletin 1947 v 41 313) by intracoeccal inoculation of 0.2 to 0.4 cc. of *E. histolytica* culture material. The present authors point out that while numerous shallow ulcers were produced in these rats which have a restricted parasite population on account of their age nothing resembling the deep disk-shaped ulcers seen in human infections was encountered. The inoculated amoebae were found to have ingested bacteria, but rarely red cells, and cysts were scanty. Natural infections of the experimental rats with an amoeba not distinguishable in fresh preparations from *E. histolytica* caused difficulty. It was believed that infection arose from cysts passed by hamsters housed in the same room. With suitable precautions, infection of the rats could be a coded. [FULTON & JONES had difficulty with similar infections in rats while carrying out amoebicidal tests and have recently reported (this Bulletin 1948, v 45 430) the results of a survey of amoebic infections in laboratory rodents—white rats, cotton rats, hamsters and Orkney voles separately housed were found to be infected very early in life, about 50 per cent. in the case of white rats before weaning. The cotton rats had been isolated since coming to Britain.] Differences in infectivity of human strains of *E. histolytica* for these young rats were noted and the infection rate in different experiments varied from 80 to 100 per cent. Drugs were generally administered in the diet for 8 days, but if it were rendered unpalatable in a promising case drug dosage by stomach tube was resorted to. The criterion of activity of a drug was the presence or absence of amoebae in the rat caeca after treatment. The macroscopic appearance of that organ was also taken into consideration. Controls were used in all experiments. The results for a series of standard amoebicides tested by both methods is given in tabular form. Emetine proved the most active drug in both cases (based on dosage given) and the relative activity of the others was in the same sequence in both tests but this was not true for all drugs. The calculation of chemotherapeutic indices showed that the curative dose of emetine was close to the toxic dose. Diodoquin had the best therapeutic index.

II A number of compounds based on structures derivable from emetine were previously synthesised by PYMAN and collaborators but proved inactive against *E. histolytica*. The present authors have prepared and tested two series of secondary diamines of the general type  $\text{Ph} \cdot \text{R} \cdot \text{N}(\text{H}) \cdot \text{N}(\text{H}) \cdot \text{R}' \cdot \text{Ph}$  (phenylalkylamine series) formally related to emetine, in which Ph represents a benzene ring, R a chain of  $\text{CH}_2$  groups. This chain was varied in length and structure and different substituent groups were introduced to the benzene ring. In a second alkylamine series the phenyl groups were omitted. The test methods were similar to those employed in Part I above. The results are given in very condensed form in a table and include those for tests carried out on certain trypanosomal, leishmanial and malarial infections. There is also a chemical section and in order to appreciate the effort involved in these researches the original should be consulted. Certain derivatives in the phenylalkylamine series showed activity both *in vitro* and *in vivo* and the authors discuss the effect of different substituents as well as of variations in length of the methylene chain. Broadly speaking, the results for the alkylamine series were similar. The difference in activity between soluble and insoluble salts of the bases including both the sodies was not significant. None of the compounds was so active as emetine many were irritant and it appeared that clinical trials were not justified.

III PYMAN (Rep. Brit. Ass. 1947 107 57) reported that 1,16-bis (di-n-amylamino) decane ( $\text{C}_{12}\text{H}_{25}\text{N}(\text{C}_5\text{H}_{11})_2$ ) showed high amoebicidal



activity *in vitro* Following this observation, the present authors have synthesized a number of compounds including aromatic derivatives, based on the model of the above substance and have studied the effect on amoebicidal activity of changes in its structure as well as in those of the corresponding secondary bases and certain quaternary ammonium salts. The tests are presented as in Part II above and a chemical section is included. The parent substance showed activity *in vitro* but only to a slight extent *in vivo*. Tertiary aromatic diamines of varied structure were inactive in both tests, while the corresponding secondary aromatic diamines showed slight activity *in vitro*. Secondary araliphatic amines were active to some extent *in vitro*, but not *in vivo*, and results with this series indicated that an *in vitro* test by itself is unreliable for assessment of amoebicidal action. As shown in Part I above the two types of test give inconsistent results in the case of diodoquin (a very insoluble substance). Quaternary ammonium salts proved a little more active than the parent tertiary bases.

J D Fulton

MILLER, A A & PECK, C R. Balantidial Dysentery. Report of a Fatal Case in Assam. *Brit Med J* 1948, Mar 6, 448-9, 1 fig on pl

The authors report this case because of the rarity of balantidial dysentery, especially in India, but they refer in a footnote to 10 cases, reported by SHUN-SHIN [this *Bulletin*, 1948, v 45, 84] in the island of Rodriguez, since their article was completed.

The present case refers to an Indian sepoy of 30 who died of an acute dysenteric illness three days after admission to hospital, and five days after symptoms began. The principal clinical features were pyrexia, abdominal pain, diarrhoea and dehydration. No pathogenic organisms could be found on repeated microscopical and cultural examination, but a number of parasites were found in an ulcerated portion of the pelvic colon. The disposition and morphology of these organisms are fully described, together with the histopathology of the ulcerated colon. These parasites had the typical morphology of *Balantidium coli*. The authors point out that although the clinical, autopsy and histological features of this case were similar to those often found in amoebic dysentery, the discovery of the balantidia suggested an alternative diagnosis.

H J O'D Burke-Gaffney

KIRSHBAUM, J D. Intestinal Coccidiosis. Report of Two Cases of *Isospora hominis*. *Amer J Clin Path* 1948, Jan, v 18, No 1, 58-60, 1 fig

"During the course of examining approximately 5,000 stool specimens for parasites, in a general hospital at Espiritu Santo in the New Hebrides, two infections with *Isospora hominis* were encountered. Both soldiers were members of the same company, both manifested mild intestinal symptoms of intermittent diarrhea, malaise and loss of weight, and both responded promptly to treatment. Eosinophilia was present in both patients. The oocysts and sporocysts were the only stages seen in both the fresh stool specimens and in specimens kept at room temperature for a period of sixty-six days. The cysts were easily identified in the fresh feces emulsified in water and also by the flotation method, using zinc sulfate or table salt."

## RELAPSING FEVER AND OTHER SPIROCHAETOSSES

WILLCOX, P H. Louse-borne Relapsing Fever in Persia. [Correspondence] *Brit Med J* 1948, Mar 6, 473

The writer of this letter refers to the paper of BODMAN and STEWART [this *Bulletin*, 1948, v 45, 433] in which the claim was made that louse-borne relapsing

fever had not been reported previously in Persia. He refers to a review of the subject in 1920 by WILLCOX (*Proc. Roy Soc Med.*, 1920 v 12, Sect. of Med., 59) and LEDDINGHAM (*ibid.* 81) based on experiences in the 1914-18 war during which the disease was a serious problem among British Forces in Iraq and Persia. Both typhus and relapsing fever were endemic and were commoner than enteric fever.

Louse infestation was extremely common in the Turkish army and relapsing fever was prevalent in Kut in the winter of 1915-18. British troops did not become infected until their contact with the local population and with Turkish prisoners. It is also noted that the disease occurred in the civil and military population of Bagdad in 1917 and mortality figures are given for 1,863 cases.

It is also pointed out that LEDDINGHAM (*loc. cit.*) had also demonstrated the correspondence in incidence curves for typhus and relapsing fever from 1917 onwards and in other respects, epidemiological and clinical, the earlier epidemic of relapsing fever corresponded closely in almost every detail with the 1944 outbreak.

Evidence is quoted to show that lice may occasionally be infective for typhus and relapsing fever at the same time and the case is mentioned of a medical officer who contracted relapsing fever 8 days after attending two cases of typhus.

H. J. O. D. Bunka-Galfary

BALLIF L., CONSTANTINESCO N. & CHELARESCO M. Meme. Recherche des spirochètolymphe dans la fièvre récurrente épidémique. (Note préliminaire). [Lysis Test in Epidemic Relapsing Fever] *Bull. Acad. Méd. Roumanie*, 1945, v 19, Nos. 4 & 5, 572-5.

The difficulty of diagnosing relapsing fever during the afebrile period when spirochaetes are absent from the blood led the authors to elaborate a lysis test. In this test dilutions of the patient's serum (from 1/1 to 1/20,000) are mixed with defibrinated blood from a patient heavily infected with spirochaetes, and with guinea-pig or human complement. After incubation at 36-41°C. for 2 hours, smear or thick drop films are prepared from each dilution, and are stained by Giemsa's method. The test is considered positive when the spirochaetes show numerous acidophile granules. The organisms may degenerate into indistinguishable masses of agglutinated granules or with prolonged incubation of the mixtures, may be partially or completely lysed.

If dried blood only is available, it should be mixed with an equal volume of physiological saline and the extract used instead of serum.

The antibodies responsible for this reaction can be demonstrated at least 408 days after recovery from the disease and, as noted above, they can be recovered from dried blood. The test is therefore useful in epidemiological surveys or in field diagnosis in times of epidemics. [No evidence is offered that these lytic antibodies will react with the numerous and serologically distinct relapse strains of the spirochaetes. Without such proof, any information derived from the test could have little practical diagnostic value.]

J. C. Brown

PASTOR BORJA, F. Consideraciones sobre las secuelas oculares en la Lepra recurrente. epulemia de los años 1943-1946 en la Zona de Protectorado Español en Marruecos. [Ocular Sequelae of Relapsing Fever seen in the 1945-46 Outbreak in Spanish Morocco.] *Med. Cuadern. Madrid* 1945, Feb. 1, 11 v. 2, 86-87.

The author states that though much has been written on relapsing fever few have referred to the eye complications and sequelae of this disease. In the louse-borne outbreak of 1945-46 he observed certain cases which he wishes to

place on record and he refers in the present article to seven of them. The complications and sequelae mentioned are subconjunctival haemorrhage and purulent conjunctivitis, iritis and irido cyclitis and uveitis, occasionally bilateral, more often unilateral and affecting nearly always the right eye. He also saw cases, one severe, of papillitis, with pallor of disk and some atrophy. The Wassermann reaction was not tried in all cases and may have been positive, but by no means in all. The conclusion is that the lesions were due to the relapsing fever and not to syphilis. The author is of opinion that if the infection were treated properly in the early stages with adequate doses of novarsenobenzol these complications might be avoided.

H Harold Scott

DAVIS G E. A Note on the Larval Stage of the Argasid Tick *Ornithodoros moubata* (Murray) 1877. *J Parasitology* 1947 Dec v 33 No 6 495-6

## LEPROSY

DOULL, J A, GUINTO, R S, BANCROFT, Huldah & RODRIGUEZ J N. Historical Inquiry as a Method of estimating the Trend of Leprosy. *Internat J Leprosy* Cleveland, Ohio 1947, Oct-Dec, v 15, No 4, 369-77

The data used were collected in the municipalities of Cordova and Talisay in the province of Cebu, Philippine Islands, a detailed history being obtained for every household, including, to the utmost extent, all births, deaths, other entries and exits and the occurrence of leprosy. Sufficiently complete records were obtained for 3,204 families including 21,791 individuals 335,016 person-years of exposure and 402 cases of leprosy (of which 261 were lepromatous and 141 neural or mixed). When the period of observation is divided broadly into years prior and years subsequent to January 1st 1915, there is no evidence of any change in the total incidence rate. In the later years, however, the milder forms of macular and neural leprosy would have been more frequently observed than in the earlier period. Limiting the comparison to the lepromatous type reveals a lower rate post-1915. A more exact comparison is made by taking persons born between 1896 and 1910, and calculating their experience up to 1920, and comparing them with individuals born between 1911 and 1925, and calculating their experience up to 1935. After adjustments for age differences in the populations at risk, the resulting incidence rates of lepromatous leprosy per 1,000 person-years are: born in 1896-1910, followed to 1920, males 1.59, females 0.78, both sexes 1.18; born in 1911-25, followed to 1935, males 0.78, females 0.31, both sexes 0.54. The later born have rates only some half those of the earlier born. Further analysis of these two groups was made to show whether this downward trend occurred in leprous households as distinguished from the total population. Only those who were known to have been living in household association with lepromatous leprosy were considered as exposed and their experience was contrasted with that of those for whom no history of exposure to any type of leprosy could be ascertained. To make allowance for the incubation period, exposures only to 1915 for the first group and only to 1930 for the second were counted. The resulting rates, adjusted for age, and per 1,000 person-years were as follows: Household exposure: earlier period, males 12.8, females 9.5, both sexes 11.3; later period, males 6.3, females 3.0, both sexes 4.7. No household exposure: earlier period, males 0.80, females 0.46, both sexes 0.63; later period, males 0.43, females 0.19, both sexes 0.32. The relative reduction is slightly greater in the leprous households.

Compulsory segregation was introduced in 1907 and the observed lower rates are in accord with the view that this may have been a factor. The experience is, however, relatively small and other environmental changes took place concurrently—in particular a rise in the standard of living—so this interpretation of the trend is not justified.

J. Bradford Hill

NEW P. Need for a Study of Social Components in Leprosy. *Internat. Med. Abstracts & Reviews*, Calcutta, 1947 Nov. v. 2, No. 3, 161-3.

## HELMINTHIASIS

RAI, B. B. Some Misleading Cases of Helminthia Infestation. *Indian M. J. Gaz.* 1947 Sept. v. 82, No. 9, 538-9.

VOX BRANT T. & FILES, Virginia S. Chemical and Histological Observations on the Influence of *Schistosoma mansoni* Infection on *Australorhynchus glabra*. *J. Parasitology* 1947 Dec. v. 33, No. 4, 478-82. (19 refs.)

"Infection with *Schistosoma mansoni* does not interfere seriously with the storage of fat in the body of its invertebrate host, the small *Australorhynchus glabra*. The latter's oxygen consumption also remains normal. Infected snails have however a reduced polysaccharide content and this reduction is a result of a diminished storage both in parasitized and non-parasitized organs. Whether this decrease is due to an impaired carbohydrate digestion and reabsorption or to a toxic action by the parasites is not clear. The possibility that it is due to the food consumption of the parasites has not been ruled out completely.

KIESER, J. A. Schistosomiasis: an Educational Problem. *South Africa M. J.* 1947 Nov. 22, v. 21, No. 22, 851-3.

In this short paper the author stresses the deleterious effect of schistosomiasis [S. haematodes m.] on intelligence and vigour. The mental symptoms are so monotonously uniform in character that a diagnosis of schistosomiasis could almost be made on them alone. In children they are forgetfulness, indifference to punishment, apparent laziness and a disinclination to mental exertion combined with a sometimes very marked nervous irritability, obstreperousness and mental fatigue. This condition may be so serious that the child may be in danger of certification as mentally deficient.

Several illustrative cases are quoted in children and young adults. Successful treatment removes these disabilities very effectively.

Charles H. Mounts

BLAIR, D. M., HAWKINS, F. & ROSS, W. F. The Effect of Miracidin on Human Schistosomiasis. *J. Med.* 1947 Dec. 20, 911-1.

Miracidin is the hydrochloride of Miracid; see this *Bulletin* 1948, v. 45, 167 and has been claimed by HARTMAN and GONNERT to be effective against infections with *Schistosoma mansoni* in mice and monkeys. The authors after two of them had investigated its pharmacology and to a high degree in monkeys and man, tried it on 47 patients in Southern Rhodesia infected with *S. haematodes m.*, *S. mansoni* or both.

The drug was given by the mouth as uncoated tablets, one each day after the middle meal for 8 days each week up to a maximum of 20 doses. Doses varied: children were given 100, 300 or 750 mgm. at a time, the three adults received doses of 200 mgm. In urinary doses of 50 mgm. were given to all patients to exclude schistosomiasis. The drug was well tolerated, but these doses approach

the known maximum tolerated dose for repeated administration, namely 200-300 mgm per diem

Results were poor Eight weeks after cessation of treatment only 9 of 40 with *S. haematobium*, and 2 of 11 with *S. mansoni*, were not passing eggs

This is a preliminary paper, details are to be published elsewhere

Charles Wilcocks

KHALIL, M & HALAWANI, A Cloroben as Snail Poison for Control of Bilharziasis—its Danger to the Rice Plant *J Roy Egyptian Med Ass* 1947, Sept, v 30, No 9, 454-60

Cloroben is an American preparation recommended for killing aquatic plants and snails Analysis indicated that it contains 61.3 per cent of ortho-dichlorobenzene as an emulsion The authors found that 50 parts per million would kill *Bulinus truncatus* and *Planorbis boissyi* in 2-3 days, but that this concentration was lethal to fish (*Gambusia*) and to rice Moreover, it is (no doubt) toxic for man and domestic animals For these reasons the authors have issued a warning against the use of this substance in small control Copper sulphate, which has been found to have a beneficial effect on rice fields by killing the algae which cause one of the important diseases of rice, remains the chemical of choice for this purpose

Charles Wilcocks

LIPPINCOTT, S W, ELLERBROOK, L D, RHEES, M & MASON, P A Study of the Distribution and Fate of Antimony when used as Tartar Emetic and Fouadin in the Treatment of American Soldiers with Schistosomiasis Japonica *J Clin Investigation* 1947, May, v 26, No 3, 370-78, 5 figs

American soldiers numbering 138, who had been infected with *Schistosoma japonicum* while serving in the Philippines and were still passing eggs in their faeces in spite of treatment, were given one or more courses of tartar emetic or Fouadin, equivalent to 45 mgm Sb on alternate days The latter was given intramuscularly and tartar emetic was given intravenously till a total of approximately 570 mgm of Sb was reached Estimations of Sb in body fluids, as well as of the amount and rate of excretion in urine and faeces, were made on some patients during and after treatment by the Rhodamine B method of MAREN (*Bull Johns Hopkins Hosp* 1945, v 77, 338) whereby a red Sb-dye complex is formed By this means, 0.5 microgramme of the element could be estimated in the absence of iron Towards the end of treatment, the level in plasma was approximately 100 microgrammes per litre after both drugs Twenty-eight days later, only one-fifth of that amount was present The concentration in red cells was consistently higher than in plasma The urinary excretion towards the end of treatment was somewhat higher after Fouadin, being then approximately 10 mgm per day and 2 mgm daily in faeces Antimony was still detectable 100 days later in both excretions A small concentration of Sb was present in bile Of 33 patients treated with Fouadin, 82 per cent who remained under observation had ova in their faeces 3 months later and a similar percentage were passing ova after a second course The relapse rate was 19 per cent in 59 patients after a course of tartar emetic

J D. Farrer

WRIGHT, W H, BAUMAN, P M & FRY, N The Control of Schistosomiasis Japonica VI Studies on the Chemical Impregnation of Uniform Cloth as a Protection against Schistosomiasis Japonica *Amer J Hyg* 1946, Jan, v 47 No 1, 33-43

These studies were carried out by members of the Commission on Schistosomiasis, Army Epidemiological Board, United States Army Studies Nos

I, II III and IV have already been noted in this Bulletin while No. V has not yet been published.

The experiments and observations recorded in Study No. VI were designed to ascertain if some method could be found for impregnating the socks and trousers of combatant troops in order to afford protection to the lower parts of the body which in combatant operations would be most exposed to the danger of infection by cercariae. The experiments were carried out with various types of Army cloths which were soaked in the chemical to be tested, and then wrung out and subsequently dried. After each test, the cloths were washed with a rather more thorough technique than is usually employed by the average enlisted man to ascertain if any effectiveness had been dissipated through the washing process. Each stage in the process of impregnation and subsequent washing was carried out under carefully standardized conditions, which included calculations on the amount of the chemical taken up by the treated cloth. The resistance to penetration by cercariae of the impregnated cloths, was ascertained before and after each washing by experiments with animals but owing to the large number of drugs submitted for testing, and the relatively few suitable animals a reliable preliminary screening by simple tests was necessary. For this purpose a measured piece of the previously impregnated cloth was placed in a Petri dish, together with 4 cc. of water for 10 minutes. 10 cercariae were then added to the fluid and kept under observation for 30 minutes. Those compounds which showed the highest percentage of kill were selected for the animal tests which were of two types. In the first, the impregnated cloth was stretched tightly over a small wire basket, and the animal was placed in this cloth-covered basket which was then stood on tared supports in a vessel containing 600 ml. of water to which 3,000 to 5,000 *S. japonica* cercariae had previously been added under these conditions, about 200 ml. of the water in the bath penetrated the cloth. Exposure was for 45 minutes and samples were taken from under the cloth after 20, 30 and 40 minutes, in order to determine whether the cercariae had penetrated. In the second method, test and control animals were anesthetized, and a small amount of water containing 500 shed cercariae was made into a pool on the cloth to be tested which was applied directly to the shaded surface of the animal's abdomen. After 45 minutes exposure the cloth was removed and the animal kept under observation for 26 days or longer after which it was destroyed and examined for *S. japonicum*. In addition to these tests of impregnated cloths the writers carried out a limited number of experiments with untreated uniform cloth, and with certain types of water repellent garments issued to the troops.

The authors summarize their results as follows:—

"To determine the value of unimpregnated clothing as protection against the acquisition of schistosomiasis japonica, in vitro and in vivo tests were carried out with 31 compounds or combinations of compounds. Types of uniform cloth tested included 8-ounce cotton suntan trouser cloth, herringbone twill cloth, olive drab woolen trouser cloth, cotton gloves and thin socks. A total of 337 animals was utilized in the exposure tests. A number of the compounds were discarded after in vitro screening tests while others failed to give good protection on the animal tests.

"An emulsion of 4.5 per cent benzyl benzoate with 0.5 per cent Tween 80 in water proved to be the most effective compound. Cotton trouser cloth and herringbone twill cloth impregnated with this emulsion provided protection through 4 washings of the cloth. Dibutyl phthalate in 5 per cent emulsion with Tween 80 in water afforded protection with cotton trouser cloth, herringbone twill cloth and olive drab woolen trouser cloth after two washings of each

type of cloth. There is reason to believe that this compound might be equally effective or more effective than benzyl benzoate. Good results were obtained also with the gas protective chemical,  $CCl_4$  (this is not a chemical formula but a secret designation). This compound protected through two washings of herring-bone twill, cotton glove material and cotton socks. Since the latter fabric is easily penetrated by schistosome cercariae the protection afforded by the chemical is of considerable significance and indicates that it might persist even after addition of washings.

The impregnation of clothing with certain water repellent compounds gives good results in some instances. However, this protection was gradually lost when the cloth was washed. In general, such compounds give results inferior to those obtained with nontoxic compounds.

The relative degree of protection afforded by various types of uniform cloth varied with the weave of the cloth and the amount of the chemical taken up during the impregnation process. From a practical standpoint, impregnated woolen uniform cloth would provide protection over a longer period of time and after more washings than either the cotton uniform or the herring-bone twill cloth. The latter would appear to offer the best protection against schistosome cercariae of the 3 standard types of uniform cloth.

WRIGHT W. H., BULLOCK P. M. & LEE N. The Control of Schistosomiasis Japonica VII. Studies on the Value of Repellents and Repellent Ointments as a Protection against Schistosomiasis Japonica. *Proc. J. Hyg.* 1948 Jan. 47 No 1 11-52 1 fig.

The experiments recorded in this paper were designed to supplement cloth impregnation experiments described in the previous paper and to develop a method for protecting the unclothed parts of the body against schistosome cercariae. Liquid preparations although they protected when applied undiluted and allowed to dry on the skin proved less satisfactory than the various ointments which were used in 16 experiments on 348 mice exposed to infection with the cercariae of *S. mansoni* and *S. japonicum*. In the case of animals exposed to *S. mansoni* the vertical immersion of the rodent and in the water proved satisfactory but owing to its surface haunting habits other methods which are fully described by the authors had to be used in the experiments with *S. japonicum*. All of the ointments employing dimethyl phthalate dibutyl phthalate benzyl benzoate Rutgers 612 Indalone or 2-phenylcyclohexanol either singly or in combination in various types of bases protected all of the experimental mice with the exception of the ointment containing copper silicate dimethyl phthalate and Rutgers 612 and the ointment containing 5 per cent of dimethyl phthalate and 5 per cent of Rutgers 612. Copper silicate alone also failed to protect although copper acetate 2 per cent afforded protection against infection as did a combination of copper acetate 1 per cent dimethyl phthalate 5 per cent and Rutgers 612 5 per cent. Two of the ointment bases in themselves offered little resistance to the cercariae, so that the protection conferred by the repellent ointments is not merely mechanical. It is clear from the results of these carefully conducted experiments that certain of the repellent ointments which were tested are of considerable value in protecting individuals exposed to schistosomiasis. The authors point out however, that many additional tests are needed, particularly as regards the length of time such ointments remain effective during continuous exposure to water or under conditions causing copious perspiration.

R. M. Go

microfilariae. The results of surveys made in this and other places are shown in the table.

Locality	Positive skin smears, per cent.	Nodules, per cent.	Blindness, per cent.
Sush Rest-house	80	3-4	Under 1
Raffia-River Bo	8	4	4-5
Raffia-Park	50	20	This probably includes all three localities
Paili	25	3	
Pongo	90	46	
Wau	10	—	10 Reported low

The number of persons examined was usually between 30 and 80. The nodules were mostly on the side of the chest or near the iliac crests and great trochanters, but many patients had no nodules. The skin conditions included xeroderma, and a condition like *craw-craw*. Blindness occurs and is definitely due to onchocerciasis in some cases. It is often preceded by a period of night blindness. Hydrocele and scrotal elephantiasis are extremely common in the areas of onchocerciasis in the Sudan but *W. bancrofti* infection is extremely rare.

F Hawk &

MAZZOTTI L. & HEWITT R. Tratamiento de la onchocercosis por el cloruro de 1-diethylcarbamil-4-metilpiperazina (Hetrazan) [Treatment of Onchocerciasis by Hetrazan.] *Medicina Mexico*, 1948, Jan. 25 v 28 No. 548 39-42.

The authors following up the success recorded by SANTIAGO-STEVENS and his colleagues in filariasis due to *W. bancrofti* (this Bulletin 1948, v 45 353) have tried Hetrazan (1-diethylcarbamil-4-methylpiperazine) in 6 patients infected with *Onchocerca* in doses of 2 mgm. orally per kilo body weight thrice daily. Four took it for 15 days and two for 21 days. Cutaneous biopsy was made thrice a week for 45 days and thereafter twice weekly. Before the treatment was begun, microfilariae were numerous, as many as 60 in a specimen 6 mm. square. Within 24 hours of beginning the treatment four patients showed a generalized oedema, especially of the face and upper part of the chest with fever, general malaise, pruritus and joint pains. In these cases the drug was suspended for 3 days, by which time these symptoms had disappeared; they were regarded as allergic. Microfilariae were much fewer even after 24 hours. Biopsies during the next 6 weeks revealed in patient No. 1 one microfilaria on the 17th day, one in No. 2 on the 14th day, 5 in No. 3 between the 5th and 8th days. This patient had to leave hospital on the 17th day and on that day 6 cutaneous biopsies were carried out and all were negative. No. 4 showed 3 microfilariae on the 6th day.

The other two patients were given one-third the dose on the first day, two-thirds on the second day and thereafter the full dose for 21 days. After 48 hours and during 90 days' observation an occasional microfilaria only was seen. One of these patients had three nodules which were later extirpated. Nos. 1, 3 and 4 also had nodules which, when removed from 14 to 39 days after the drug treatment was started, were found to contain adults normal in appearance and living embryos. In one nodule the adults seemed to be normal, but microfilariae which were present in large numbers, were all dead. (See OLIVER-GONZALEZ & HEWITT below)

H. Harold Scott



- ALICATA, J E & KARTMAN, Anna Y Incidence of Oxyuriasis among a Group of School Children in Honolulu *Hawai Med J* 1948, Jan-Feb, v 7, No 3, 214-15, 2 figs

"An examination of a group of 138 children, aged  $2\frac{1}{2}$  to 7, attending school (nursery to first grade) in Honolulu, showed 31.1 per cent to be positive for pinworms on two swab examinations. Calculated on the basis of seven swabs, believed required to reveal most cases, the incidence of infection would probably be about 38 per cent. The number of positive cases was found to be equal among the two sexes. Children of Caucasian ancestry appeared to show a higher incidence of infection (40 per cent) than those of Oriental ancestry (21 per cent). The results indicate that oxyuriasis is probably common in this community and represents one of the problems of public health importance."

- OLIVER-GONZÁLEZ, J & HEWITT, R I Treatment of Experimental Intestinal Trichinosis with 1-Diethylcarbamyl-4-Methylpiperazine Hydrochloride (Hetrazan) *Proc Soc Exper Biol & Med* 1947, Oct, v 66, No 1, 254-5

Since Hetrazan has been used with good results in filariasis [this *Bulletin*, 1948, v 45, 353], it was considered worth testing it in *Trichinella spiralis* infections in white rats.

Between 1,000 and 1,300 *Trichinella* larvae were given by stomach tube and 24 hours later a course of Hetrazan was started, a dose on the basis of 200 mgm per kilogramme body-weight was given by stomach tube 3 times a day for 5 to 10 days. Rats were killed after 5, 10 and 30 days and the intestines and muscles were examined for worms and larvae.

After 5 days, an average of 91 worms were recovered from the intestines against 481 in the case of untreated controls. After 30 days the average number of larvae recovered from the muscles in the two groups of untreated animals was 31,200 and 26,100 compared with 320, 112 and 2 in three groups of animals treated for 5, 10 and 20 days, respectively.

Hetrazan is relatively non-toxic in man and it is thought possible that, as in the case of filariasis, the effective dose in man may be lower than that required in the rat.

[In the table, it is shown that after 10 days 312 worms were recovered from the intestine of the treated rats against 61 in the untreated rats. There is no comment in the text on this apparently paradoxical observation.] [See also MAZZOTTI & HEWITT, above] L E Napier

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## DEFICIENCY DISEASES

- MACNAMARA, O D The Effect of Diet and Helminthic Treatment on African School Children *Trans Roy Soc Trop Med & Hyg* 1948, Jan, v 41, No 4, 519-24

The African child in central Nigeria is undernourished, and usually suffers from helminthic infection—most commonly hookworm and urinary bilharzia. One hundred and sixty-five school-children were divided into 3 groups: a control group received no treatment of any kind; a second group was given extra food at school; the supplement was calculated to produce an adequate and well balanced diet; a third group was treated for helminths with oil of chenopodium and tartar emetic. The period of observation was 100 school days. The group which had extra food showed an average weight gain of 3 lb 10½ oz,

compared with 1 lb 10½ oz. in the control group and 9½ oz. in the group treated for worms. There was no significant difference between the groups in the gains in height. In the supplemented group, there was a significantly greater increase in chest circumference and an increase in endurance as tested by hanging from a bar. General health was also better in this group and signs of vitamin deficiency disappeared. There was no improvement of general health in the group given antiparasitic treatment.

J. C. Waterson

REID J. A. & WILSON T. Report on Nutrition, and Diseases of the Main Causes of Death, "F" Force, Thailand. *J. Roy. Army Med. Corps* 1947 Oct., v 89 No 4 149-85.

The story of "F" Force Thailand, is now fairly well known. As a result of appalling living conditions, forced labour, cholera, dysentery, malaria and deficiency disease 44 per cent. of the force of 7 000 men died in a year. Anyone who reads this paper must feel admiration for the authors and those who worked with them when it must have seemed unlikely that any of them would ever return to civilization, they continued to collect data and to keep records in face of immense moral and material difficulties.

Major Reid and Captain Wilson give a general description of the conditions to which "F" Force were exposed but their chief emphasis is on nutrition. The diet issued by the Japanese consisted mainly of highly-milled rice with some dried beans. Meat, when provided, was usually in a state of decomposition. Supplements were almost unobtainable but in some camps green leaves and wild gourds were eaten. Analysis of the diet shows that 80 per cent. of the energy was derived from carbohydrate, and 90 per cent. of this from highly milled rice. The protein intake was in the region of 30-50 gm., mainly of vegetable origin. Fat and vitamin A were almost completely absent. The average daily amounts of vitamin C, riboflavin and nicotinic acid were about 3.07 and 6 mgm. respectively. The thiamin non-fat-calorie ratio (the total amount of thiamin in the diet (mgm.) divided by the non-fat calories never exceeded 0.3 and was usually below 0.4. The value given by WILLIAMS and SPIES as the minimum necessary to protect against beriberi is 0.3. It is not surprising that under these conditions beriberi was widespread and accounted for 13 per cent. of the deaths. 11 per cent. more were attributed to beriberi complicated by dysentery. The diagnosis of beriberi was based mainly on the presence of oedema, which was almost universal. Acute cardiac beriberi was common, but the dry neuritic type was rare.

Another very common condition, attributed to malnutrition, was tropical ulcer. The cases improved, and were less frequent when rice polishings became available. A most important observation was the rarity of diseases caused by deficiency of the B<sub>2</sub> vitamins, such as scrotal dermatitis and glossitis, painful feet, paraplegia and amblyopia. Many of the members of "F" Force had suffered from these conditions while in Changai. Men who had glossitis or scrotal dermatitis when they left Singapore recovered on the train journey, or soon after reaching Thailand. The suggestion has been made that in some way this may be related to the low calorie intake. BRUGGES in Singapore (this *Bulletin* 1947 v 44 114) observed that signs of riboflavin deficiency appeared mainly in the relatively well-nourished.

The authors state their conclusions as follows: "In our opinion—and we think it is shared by every M.O. on this expedition—the gross inadequacy of the Thailand diet in conjunction with the merciless compulsion to excess exertion, outweighed in importance all other causes of death."

[This opinion is of value, since there are still many parts of the world where the population is exposed to similar if less serious conditions of malnutrition.]

and disease Any experience is important that indicates where to attack the vicious circle that these acting together, so easily set up In the case of "F" Force, it is permissible to speculate that some of the cases of diarrhoea diagnosed as dysentery may in fact have been caused by malnutrition (See MCKENZIE, this *Bulletin*, 1940 v 37, 809) ] J C Waterlow

EPSTEIN, S Observations on Beriberi Heart Disease *Amer Heart J* 1947, Sept, v 34, No 3, 432-40, 5 figs [23 refs]

A case is described of a middle-aged woman, who for many years had been living on large amounts of alcohol and very little food On admission to hospital she had signs of congestive heart failure and a macrocytic anaemia with achlorhydria Both conditions responded to treatment with vitamins and a full diet

The diagnosis of beriberi was based on the following evidence

- 1 the dietary history,
- 2 the presence of signs of malnutrition (glossitis cheilitis) but not neuritis
- 3 the presence of cardiovascular changes considered to be characteristic of beriberi enlargement of the heart, increased output, pistol-shot sounds, raised venous pressure and low voltage in the electrocardiogram,
- 4 the response to treatment, described as specific 100 mgm of thiamin, 150 mgm of nicotinic acid, and 200 mgm of ascorbic acid were given daily, together with vitamins A and D, blood transfusions and a full diet

[In recent years workers in America have attempted to define criteria for the early diagnosis of cardiac beriberi (see BLANKENHORN, *et al*, this *Bulletin*, 1946, v 43, 945) This is difficult, because the cardiovascular changes are not specific In the case described above they could, as the author admits, be attributed to anaemia—an explanation which is not ruled out by the fact that the condition of the heart improved before that of the blood (see HUNTER, A, *Quart J Med*, 1946, v 15, 107) In the present state of knowledge there seem to be only two convincing tests for beriberi, a dramatic response (within a few hours) to parenteral administration of thiamin, and an increase in pyruvic acid in the body fluids, either at rest or after mild exercise (see LU and PLATT, *Biochem J*, 1939, v 33, 1538) ] J C Waterlow

## SPRUE

COOKE W T FRAZER, A C, PEENEY A L P, SAMMONS, H G & THOMPSON, M D Anomalies of Intestinal Absorption of Fat II The Haematology of Idiopathic Steatorrhoea *Quart J Med* (n s) 1948, Jan, v 17, No 65, 9-24, 2 figs on 1 pl [65 refs]

This paper represents a study of the haematology of 45 cases of idiopathic steatorrhoea and contains observations on the aetiological factors concerned. Diagnosis has been made on the history, the presence of a characteristic haematological and abnormal electrolyte picture excess faecal fat, flat glucose and chylomicrograph curves and low fasting serum lipoids

In 42 patients, the presence of a fat absorption defect was determined by a fat balance technique Most hypotheses concerning the anaemia in idiopathic steatorrhoea have been based upon the unitarian theory of the aetiology of the macrocytic anaemias, but the similarity between the anaemias of steatorrhoea and pernicious anaemia are superficial and a close relationship between them could not be established in this series Although minor differences may be seen

in the morphology of the peripheral blood and in Price-Jones curves, more significant differences are in the high incidence of free hydrochloric acid in the gastric contents and the demonstration of intrinsic factor in the gastric juice of one patient. Furthermore refined liver extracts did not produce a reticulocyte response in the blood picture even in those presenting sternal marrow findings identical with those in pernicious anaemia.

Minor degrees of iron-deficiency were remedied in some but the finding of a low colour index or low mean corpuscular haemoglobin concentration was not an indication that such blood pictures could be corrected by administration of iron alone. A consistent feature has been decreased fragility of red cells to hypotonic saline similar to that noted in a number of anaemias. The rapid fall in red cells and haemoglobin that may occasionally be noted suggests a haemolytic process comparable with that demonstrated in pernicious anaemia, and the finding of increased erythropoiesis in the bone-marrow with relatively static peripheral blood counts might also be regarded as evidence of a maturation defect.

Serum-bilirubin levels have not been markedly abnormal. Total pigment excretion in the urine and faeces was within normal limits. There is therefore little evidence of increased red cell destruction in idiopathic steatorrhoea.

The conception that faults in fat absorption may give rise to blood disorders opens up wide fields of investigation. The lack of correlation between the haematological improvement and the fat absorption defect and the occurrence of death with a relatively normal blood picture might be considered as evidence against the anaemia being secondary to the underlying fat absorption defect. It can be shown, however, that there are aetiological differences between the various types of defect. Thus the absorptive defect persists in idiopathic steatorrhoea, whereas in sprue and pellagra the defect may disappear entirely. It seems that qualitative changes in fat absorption may occur in the absence of any alteration in the total amount of fat absorbed. It may be as is suggested by the recent demonstration of the action of folic acid and thymine that the reticulocyte responses have been due to the replacement of temporary deficiencies of various accessory factors which were conditioned by or dependent on, an underlying fault not affected by treatment.

[For Part I see this *Bulletin* 1948, v 43 846.]

P. M. LOW-BAS

I. DAVIDSON, L. S. P. & GIRDWOOD R. H. The Imbalance of Vitamins with particular reference to Folic Acid. *Lancet*. 1948, Mar 6 360-63 (15 refs.)

II. *Lancet* 1948 Mar 6 371 2. Folic Acid and the Nervous System.

I. In two patients with pernicious anaemia and three with sprue who were treated with folic acid, various signs of deficiency of the vitamin-B complex arose. These signs did not improve until folic acid was supplemented with, or superseded by, liver or liver extracts. The authors writing from the University of Edinburgh, have found neurological changes in 8 out of 23 cases of pernicious anaemia treated with folic acid alone.

The three cases of the sprue syndrome are of special interest. The first was in a patient with idiopathic steatorrhoea who developed a mild peripheral neuritis; treatment with folic acid coincided with steady deterioration of neurological features, despite improvement of assimilation from the alimentary tract and oral and parenteral administration of large amounts of thymine. In addition, signs of riboflavin deficiency developed. The second appeared to be a case of tropical prue in a patient from N. Africa in whom partial ileo-tomy had been performed for megacolon. While the patient was undergoing folic acid treatment signs of peripheral neuritis developed. When L. was

treated with proteolysed liver by mouth supplemented with intramuscular injections of thiamin, riboflavin and nicotinic acid by the mouth, signs and symptoms of peripheral neuritis steadily improved. The third [referred to below] was a case of tropical sprue from India. On folic acid being given by the mouth, 50 mgm daily, the intestinal symptoms responded rapidly, but within a week a fiery red rash of butterfly distribution appeared on the patient's face, cheilosis, and glossitis also occurred. There was severe mental depression. No response was obtained to nicotinic acid, but combined therapy of folic acid and parenteral liver caused the dermatitis to subside in four days. When liver injections were discontinued, the dermatitis recurred, but it disappeared when folic acid was discontinued. The implications of this curious anomaly and the possible underlying principles have already been discussed.

ii. One of the surprises of treatment with folic acid has been the complete failure of this anti-anaemic substance to influence the changes in the nervous system that occur in many patients with pernicious anaemia.

It is possible, as HURST argued, that changes in the haemopoietic and nervous systems are due to deficiencies of different factors, both in some way connected with achlorhydria. In support of this, it is to be noted that some patients with pernicious anaemia have no detectable involvement of the central nervous system, and others with combined tract degeneration of the spinal cord who show no anaemia. But even this does not explain why these nerve changes should appear in those whose blood has been restored to normal by folic acid. This acute cord involvement is something quite new. But when the correct treatment with liver is substituted, recovery of the nervous system is quicker than is normal in the naturally occurring combination of pernicious anaemia with postero-lateral cord sclerosis. Some have even suggested that folic acid may in some way interfere with the metabolism of the conducting tissue of the nervous system.

For the curious action of folic acid in reproducing pellagrous symptoms, including dermatitis in a sprue patient reported by DAVIDSON and GIRDWOOD [above], different explanations are suggested.

In the United States, ROSS, BELDING & PAEGEL, (*Blood*, 1948, v 3, 68) observed that, on the whole, the patients who exhibited signs of posterolateral tract disturbance were those receiving the larger doses and that it persisted as long as folic acid was taken. Is it possible that folic acid denies to the nervous tissue an essential substance, in much the same manner as sulphonamides block the utilization of *p*-aminobenzoic acid in bacterial metabolism? Davidson and Girdwood think that treatment with one member of the vitamin B complex may sometimes bring out signs of deficiency of others, and that disproportion of vitamin B members might be responsible for the appearance of peripheral neuritis and of pellagrous symptoms in steatorrhoea and that some similar mechanism might explain damage to the posterolateral tract during treatment of pernicious anaemia with folic acid. Liver extract may act by "liberating" the appropriate vitamins from "conjugated" forms.

At the present moment, the hypothesis of Ross *et al* in the United States appears the most likely, as the Edinburgh series of cases of steatorrhoea had possibly multiple deficiencies. The connexion between subacute combined cord degeneration and vitamin B deficiency is not proved, as was shown by Spies's patients with nutritional anaemia who were kept on a deficient diet and treated with folic acid (SPIES *et al* this *Bulletin*, 1948, v 45, 462).

The lesson is clear—namely that, whether alone or with liver extract, folic acid must not be given to patients who show any signs of involvement of the nervous system, and the idea that folic acid and liver extract together are preferable to liver alone is negated. [See also this *Bulletin* 1948, v 45, 360.]

P Manson-Bahr

- JUKES, T. H. & STOKSTAD, E. L. H. Pteroylglycine Acid and related Compounds. *Physiol. Rev.* 1948 Jan. v 28, No. 1 51-103, 3 figs. [306 refs.]

## HAEMATOLOGY

- ETES, J. E., FARRAR, E. M. & STICKNEY, J. M. Ulcers of the Leg in Mediterranean Disease. *Blood* 1948, Mar., v 3, No. 3 302-3 2 figs.

"Ulceration of the skin of the legs may occur in Mediterranean disease (Cooley's anaemia). Such ulceration cannot be distinguished grossly from that occurring in sickle cell anaemia and congenital hemolytic icterus. The outstanding histologic feature (noted at biopsy of one of these ulcers) is the prominent deposition of iron in the cutis.

- SLATEX, E. F. Familial Erythroblastic Anaemia (Cooley's Anaemia). Report of Possible Cases in Two Filipino Brothers. *Hawaii M J* 1948 Jan. Feb. 7 No. 2 210-13, 1 fig. [18 refs.]

- SIL, A. E. M. Absence of Sickling Phenomena of the Red Blood Corpuscles among Brazilian Indians. *Science*, 1948, Feb. 27 221 - [11 refs.]

## VENOMS AND ANTIVENOMS

- MOLE, R. H. & EVERARD, A. Snake-Bite by *Echis carinatus*. *Quart. J. M. S.* 1947 Oct. New Ser. v 16, No. 64 291-303 2 figs. [20 refs.]

This is an account of clinical and laboratory findings in two cases of snake bite treated in the R.A.F. General Hospital, Karachi. The snake responsible for the bite was not positively identified in the first case although strong circumstantial evidence is provided that it was *Echis carinatus*. This snake was identified in the second case.

The first patient was bitten in the right ankle and did not report until 8 hours later, by which time the right foot and leg up to the knee were swollen and patchily discoloured by extravasated blood. The popliteal pulse was not palpable. The patient collapsed after the intravenous administration of 5 cc. polyvalent antivenom serum (hasauli). His condition deteriorated and by the second day the coldness and pulselessness of the affected foot suggested that gangrene was developing. Expectant treatment was carried out, and in view of continued haemorrhages (urine and faeces both contained blood) blood transfusion was started. The patient improved but on the fourth and fifth days, although the circulation in the right leg had improved, haemorrhages from the various skin lesions and in the urine became increasingly profuse. At this stage as on the second day blood platelets were almost absent. He subsequently had two attacks of pain and restlessness which were considered to be due to pulmonary infarcts, and suffered two extensive spasms of the limb and trunk but on the sixth day he improved and the bleeding stopped suddenly. An hour later transfusion was stopped. Blood was present in the urine until it disappeared suddenly on the eighth day. Consciousness was interrupted by a mild paralytic state.

On the second day the platelets were too few to count and plasma fibrinogen was reduced to less than 10 mm. per cent. Clotting time of serum blood was greatly increased or normal and the clot showed only a few tiny fibrin

strands " The icteric index was 11 The platelet count was still very low on the third day, but after that began to improve By the fifteenth day, both the platelet count and the fibrinogen content of plasma were normal The icteric index rose to 22 on the sixth day and was 12 on the fifteenth The haemoglobin percentage was 96 on the second day, 70 on the third, 75 on the sixth and thereafter rose to normal

Benzoate detoxication tests were carried out on three occasions in the first case over the second three weeks of the illness The results indicated 'prolonged impaired hepatic function' Similar tests on the third day demonstrated considerable reduction in excretion of hippuric acid, this was still evident to a much less marked degree on the 20th day

The second patient was bitten in the thumb The snake was killed and identified The bite wound was incised and an intermittent tourniquet applied to the arm within 15 minutes Half an hour later, 10 cc polyvalent antivenin (? Haffkine) was administered intravenously Five hours after the bite the patient complained of abdominal pain and retching A further dose of antivenin was given and blood examinations were made Recovery followed, but convalescence was slow Six hours after the bite, the plasma fibrinogen was normal but there were too few platelets to count Eight hours later, platelets numbered 15,000 per cmm, and thereafter returned to normal by the third day

The authors suggest that *Echis* venom has a pronounced effect on liver function and on "capillary function", as illustrated by the haemorrhages and thrombocytopenia Because in the first patient the bleeding into the urine continued for two days after bleeding from other sites had stopped, they suggest that the venom is excreted by the kidneys In spite of increased clotting time, they regard venous thrombosis to be the cause of the "intensity of the oedema and absence of any detectable circulation", in the affected limb in the first patient No fibrolysin was detected, so that the lack of fibrinogen was probably related to failure of production in the liver The platelets were probably being produced in normal numbers, but "were consumed in some way directly or indirectly by the action of venom"

In discussing treatment, the authors stress the importance of administration of antivenin Continued blood transfusion is recommended in order to maintain blood volume They advise forcing fluids by mouth to induce a high urinary output, hoping in this way to assist in the elimination of the venom

[The important point made in this paper is the emphasis on the value of early and continued blood transfusion It is a pity that the snake was not identified in the first case The arguments advanced in support of the view that the venom is excreted in the urine are surely not valid The evidence merely indicates severe damage to the renal vessels In any case it is unlikely that venom is excreted as such The findings in the blood are hardly compatible with the suggestion that venous thrombosis occurred in the leg of the first patient

The statement that "a British pathologist in West Africa was bitten on the finger by a Russell's viper" is remarkable in that, so far as the reviewer knows there is no other record of the presence of this species (or genus) in West Africa]

B G Maegraith

MARQVARD, H Saenkningsreaktionen ved Hugormebid [Stabilizing Action of the Venom of *Vipera berus berus* on a Blood Suspension after Bites from the Viper] *Nordisk Med* 1948, Mar 19, v 37, No 12, 588-9 French (summary)

BERGENHEM and FAHREUS (1936) and Bergenhem (1938) have demonstrated the stabilizing power of lysocithin in a pre-haemolytic dose on a blood suspension *in vitro* Because of its lecithase content, cobra venom has the same

stabilizing action. In 10 hospital patients who had been bitten by *Liferia* *torus torus* 1<sup>st</sup> to 4 hours before it was found that the hyocithin formed by the lecithase in the blood suspensions were stabilized. It is believed that venom is the stabilizing substance. Antivenom serum given later than an hour after the inoculation of venom does not check the stabilizing action. Hyocithin already formed is not adversely affected by the antivenom serum but serum given half an-hour after the inoculation of venom evidently restricts the action of the lecithase because in this case the formation of hyocithin and its stabilizing action are clearly reduced.

H J O'D Burke-Gaffney

GRASSET E. Le venin de *Bitis nasacornis* son anavenin et préparation d'un sérum spécifique. [The Venom of *Bitis nasacornis* and the Preparation of a Specific Antivenom.] *Labor J. Rodhain* (Sec. Belge Méd. Trop. Brussels) 1947 Dec., 225-40 3 figs. [15 refs.]

*Bitis nasacornis* Rhinoceros Viper River Jack, the Ibele or Bata of the Belgian Congo exists over much of tropical Africa. The author has tested the toxicity of its venom on white mice guinea pigs, rabbits and pigeons by various routes, intravenous, subcutaneous and intramuscular. Comparing it with the venoms of *B. aridus* and *B. gabonica*. It is less toxic than either to mice and guinea pigs, but to rabbits it is equal to that of *B. aridus* but less than that of *B. gabonica* while in pigeons the toxicity is practically the same in all three. Death is preceded by increasing dyspnoea, convulsions and, at times, the passing of bloody fluid per anum, and at autopsy extensive haemorrhage is seen in all the organs. Animals which survive show extensive haemorrhagic oedema, necrosis and scarring at the site of inoculation. Antivenene is obtained by injecting horses with increasing doses of ana venom (venom plus serum) and a compound antivenene can be produced by inoculating with the venoms (or anavenoms) of *B. aridus*, *B. nasacornis*, *B. gabonica* and *V. jelskii* but the antitoxic action of the compound varies considerably. For example 1 cc. of a product thus prepared neutralized respectively 1 the above 22, 9.5, 23 and 2 mgms.

H Harold Scott

SURGENT Et. Abris des scorpions. [The Shelter Habits of Scorpions.] *Arch. Inst. Pasteur d'Algérie*, 1947 Sept. Dec. v 23 Nos. 3-4 203-9 7 figs.

The author studied the types of shelter preferred by the three commonest varieties of Algerian scorpions, *Prionurus australis*, *Buthus occidens* and *Scorpio maurus*. In all, 11 008 observations were made.

The scorpions were studied in experimental cages each of which was provided with a darkened and a light shelter the latter being covered with clear glass. Each type of shelter was constructed in three different forms, namely (1) horizontal platform raised 3 mm. from the ground (2) the same resting at an angle against the side of the cage, the upper end being 4 cm. from the ground and (3) the same, with the three sides closed in with cardboard (thus, in the case of the dark shelter the "penthouse" was completely obscured, while the light one was illuminated by the glass plate).

It was found in this way that 90 per cent. of the scorpions preferred the dark to the clear shelter and 60 per cent. preferred the "contact" platform to the "distant" one.

This supports the findings of JEANNE, quoted by BERLAND in his book *Les Scorpions* namely that scorpions which find a refuge under stones during the daytime like above all to have some solid body below and under them.

H J O'D Burke-Gaffney



## DERMATOLOGY AND FUNGUS DISEASES

BAKER, R. D. Tissue Changes in Fungous Disease *Arch Pathology* 1947, Nov, v 44, No 5, 459-66

In a comparison of the common tissue responses in fungous diseases, the author has chosen to subdivide the reactions into 5 groups, based upon the presence of suppuration, macrophages, giant cells, caseous necrosis and fibrosis. All these features commonly occur in North and South American blastomycosis, coccidioidomycosis and in sporotrichosis. In actinomycosis, nocardiosis, maduromycosis and chromoblastomycosis, similar reactions occur but without caseation. Suppuration is usually absent in histoplasmosis and in cryptococcosis. Acute inflammation with necrosis is prominent in mucormycosis and in aspergillosis. There is either no reaction or only a low-grade chronic inflammation in moniliasis or in dermatophyte infection, unless there is invasion of deep structures.

Presence of giant cells may be determined partly by the large size of fungal elements. The action of liberated endotoxins, and the development of hypersensitivity to such products, may influence cytological response. The chronicity and extent of fibrosis are partly determined by the persistence of living organisms, both free in tissues or within macrophages.

The author fails to demonstrate any one tissue change which is characteristic of fungous infection, whereas the diversity of both active and passive reactions is illustrated.

R W Riddell

BAKER, R. D. Experimental Sporotrichosis in Mice *Amer J Trop Med* 1947, Nov, v 27, No 6, 749-69, 10 figs on 6 pls

Groups of mice were inoculated with saline suspensions of strains of *Sporotrichum schenckii* grown on glucose agar. Intraperitoneal injection produced thin whitish plaques on the spleen and also peritoneal nodules which had increased up to 2 mm diameter by the second week, with later peritesticular caseation. Minute grey hepatic foci appeared by the third week, sometimes the lungs were involved. Gross lesions did not change after about 4 weeks. Organisms were present in large numbers in retrosternal lymph nodes and in reticulo-endothelial cells of the liver and other organs. Haematogenous dissemination occurred in the first week. Unlike the findings in human sporotrichosis, direct examination of fresh material in 10 per cent NaOH and in lactophenol blue or Gram-stained smears, showed numerous organisms almost as frequently as did cultures, which were usually positive even in mice inoculated over 100 days before. Death occurred in about 3 weeks with mainly peritoneal and hepatic lesions, or was delayed until about 12 weeks when lesions were generalized.

Injection into the hind paw produced an abscess which ulcerated in the second week. Suppuration occurred in popliteal lymph nodes and osteomyelitis developed. Organisms were readily demonstrated by microscopy and culture. Spontaneous recovery was possible or haematogenous spread caused death in 2 or 3 months.

Similar results were obtained with the use of diluted pus from human sporotrichosis. The mouse, like the rat, may be used for experimental and diagnostic work and is more readily infected than the guinea-pig or the rabbit.

R W Riddell

SANCHEZ MARLOQUIN A. & DE LOS ANGELES GONZALEZ, M. Estudio micológico de 16 casos de Esporotrichosis en la ciudad de México. [Mycological Study of 16 Cases of Sporotrichosis in Mexico City] In, *Ensayos N.º Ciencias Biol. México*. 1945, May 15 v. 4 No. 1 19-40 5 figs. [Numerous refs.]

The English summary appended to the paper is as follows:—

Sixteen cases of sporotrichosis in Mexico City are studied, classifying them in three different types: localized lymphangitic, disseminated subcutaneous and epidermal.

*Sporotrichum schenckii* (Hektoen and Perkins, 1900) was isolated and identified as the etiologic agent. The morphological and biochemical characteristics of the parasite are described, pointing out its particular pleomorphism and the impossibility of establishing taxonomic differences, exclusively on the basis of biochemical properties.

Finally, biopsies of subcutaneous nodules were performed and studied in two of the cases.

LAWRIER T. A. Localized Coccioid Oostomyelitis. *New England J. of Med.* 1948 Jan. 29 v. 238 No. 5 150-52, 1 fig. (20 refs.)

"A case of localized coccioid infection of the os calcis that did not respond to general and local therapy is presented. Amputation of the extremity was followed by highly satisfactory wound healing without further dissemination.

MENDOZA, J. T. Histoplasmosis: Report of a Case. *Monthly Bull. Bureau of Health* Manila. 1947 Jan. v. 23 No. 1 33-40 1 folding chart

"1. A case of histoplasmosis, the third of this disease diagnosed in the Philippines is reported.

"2. The etiology and manifestations of the disease are briefly described.

"3. It is probable that there are more cases of this disease here but they remain unrecognized due to lack of previous knowledge on its recognition. This case is therefore reported to make the local medical profession and the public histoplasmosis conscious."

## HEAT STROKE AND ALLIED CONDITIONS

DAILY W. M. & HARRISON T. R. A Study of the Mechanism and Treatment of Experimental Heat Pyrexia. *Amer. J. Med. Sci.* 1948 Jan. 15 No. 1 42-53 7 figs. (22 refs.)

This paper begins with a review of the literature on heat pyrexia. From this it emerges that there are three problems as yet unsolved: "why do patients stop sweating? what is the mechanism of the circulatory collapse that is first found? what is the most effective means of reducing the temperature?" In animals, the mechanism of evaporative cooling differs considerably from that of man, and therefore investigation of the first question—the failure of sweating—was not possible.

Cardio-vascular changes were studied in anaesthetized dogs in a chamber heated to 45-50 C. Arterial and venous blood pressures were recorded; the oxygen content was measured of arterial blood and of venous blood from superior vena cava, the hepatic vein and the right atrium. Total oxygen consumption

was also measured, and cardiac output was calculated by the Fick principle. As the body temperature rose, three clinical stages could be distinguished up to about 40.5°C (105°F) there was increasing excitement and the skin was flushed. From 40.5° to 42°C (105–108°F) the flush increased and petechiae appeared, hyperpnoea was extreme, movements were poorly co-ordinated. At about 43°C (110°F) convulsions and coma occurred, the flush gave way to an ashen grey pallor, with depressed respiration. As the pyrexia developed, venous pressure, measured in the right atrium, remained unchanged, arterial pressure was fairly well maintained, until the "grey" stage, when it fell to shock levels. Oxygen consumption and cardiac output rose steadily with increasing body temperature, but both fell steeply in the terminal "grey" stage. The circulation through the skin, as measured by the arterio-venous oxygen difference increased in the initial stages while that through the viscera was low. This suggested that cutaneous vasodilatation was compensated by splanchnic vasoconstriction. In the late stages the difference was reversed as a result of either injury to the thermal centres or local accumulation of metabolites, visceral vasoconstriction failed, leading to a fall in blood pressure, decreased cutaneous circulation, and death. These results indicated that the circulatory collapse caused by pyrexia was peripheral rather than cardiac.

Another series of experiments was concerned with the effects of heat pyrexia on cardiac reserve. Rats were anaesthetized, and given sudden massive intravenous infusions of saline. The venous pressure rose but quickly fell to normal again. In rats not exposed to heat it remained normal, but in rats heated to 42–43°C there was a secondary rise in venous pressure, followed by a fall in arterial pressure, and death. At autopsy, pulmonary oedema was found. From this it was concluded that heat pyrexia caused impairment of the cardiac reserve, and that in patients with pre-existing cardiac disease it might be expected that heat stroke might lead to cardiac rather than peripheral failure. In mice exposed to heat it was found that moderate doses of saline given intraperitoneally increased the duration of survival. Larger and smaller doses were ineffective. Experiments with digitals were inconclusive.

The effectiveness of treatment was investigated in rats and mice. The animals were heated to the point of coma, and then cooled. In rats, the fall in body temperature was followed by means of a thermometer inserted in the large intestine, in mice the efficiency of the treatment was estimated by the number of mice surviving. It was found that immersion in ice-water produced more rapid cooling and a higher survival rate than cooling by wetting and fanning. Recommendations for treatment are given, based on these experimental findings. [It is a pity that the limitations of animal experiments prevented the authors from extending their rigorous and careful work to the third problem—"why do the patients stop sweating?" Circulatory collapse seems to be a secondary effect of heat stroke, not a part of the condition *per se*, it is an uncommon complication in fit and young subjects, e.g. in Service personnel developing heat stroke in India or Iraq. In these patients, treatment by wetting and fanning in a cool room has proved effective, even if it does not produce the most rapid cooling [this *Bulletin* 1945 v 42 143]. Ice-water is seldom available in large quantities in the desert. In practice the most important gap in our knowledge is not of treatment, but of prevention. This gap cannot be filled until more is known about why sweating suddenly stops.]

BALMANN C & GAILLARD Blanche D E. De praktische betekenis van de functiebepaling der bloed-Epnoebarrière bij neurologische patiënten in de tropen (Estimation of Plasma Permeability of the Choroidal Barrier in Tropical Neurology) *Nederl Tijdschr v Geneesk* 1948 Mar 6, v 62 (1) No. 10 688-93. English summary (4 lines)

Discussion of the significance of the different composition of blood plasma and cerebrospinal fluid indicates that it is a physical and physiological phenomenon. The present article deals with this point and goes on to an argument which would explain "Tropical Headache" largely a hemikrania, as being due to increased function of the choroidal vascular plexus. The result of exposure to tropical conditions is given as increased permeability of the capillaries and an altered inorganic composition with increased tension of the cerebrospinal fluid. Estimation of the plasma quotient, or blood-cerebrospinal fluid ratio which normally for the Walter bromide test, should be 2.9 to 3.3 is considered to support the contention and, therefore, to indicate therapy directed towards the regulation of this functional disturbance. The test is described in detail and three tables furnish the data regarding patients tested, who were soldiers present in the tropics for only a short time. [The Walter bromide test is based on the fact that the ratio of the amount of bromide in the blood and cerebrospinal fluid is constant in normal persons, but may vary in those suffering from mental disorder.]

W F Harvey

DAVIES J N P. Pathology of Central African Natives. Mulago Hospital Post Mortem Studies V *East African Med J* 1947 Dec, v 24 No. 12, 437-49 (23 refs.)

Part V of this series deals with spirochaetal diseases in Uganda. Most attention is given to syphilis and yaws, but rat bite fever has been seen. Tick borne relapsing fever (*Ornithodoros moubata*) has long been a scourge in Uganda, but autopsy findings are not diagnostic and spirochaetes tend to disappear soon after death. Vincent's infections are frequent as primary and secondary invaders. Their relation to tropical ulcer will be discussed in a later paper. Cancerous oris is attributed to this infection.

The incidence and characters of syphilis recorded by LAMBORN (1889) and KEANE (1917) are contrasted with those occurring at present. The incidence is now lower and congenital syphilis is rare. Secondary syphilis is said to be infrequent (this appears to be a misinterpretation from a paper (*Brit Med J*, 1947 Jan. 18 88 see also this *Bulletin* 1947 v 44 527) by the reviewer). Tertiary lesions and neurosyphilis are common (for the latter statement the author quotes from an unpublished thesis so also as severe and often phagedenic chancres. Forty years ago the incidence was otherwise. It is suggested that the disease described by Lamborn & Keane was yaws not syphilis despite their reports of much congenital syphilis. The author has been informed that one doctor sees a lot of yaws—in the country round Kampala. (No mention is made of endemic syphilis, such as has been reported from other countries.)

In 2,994 autopsies (1931-1946) syphilitic lesions were recorded in 11.3 per cent (336). 90 per cent. were men. In 77 per cent. of these syphilis was the main cause of death. Aortitis accounted for 61.7 per cent. (207) neurosyphilis, 44.5 per cent. (154) aortitis with neurosyphilis 15 per cent. (53) gummata, 7.6 per cent. (26) (figures and totals do not tally). The findings in 1946 were similar. Aortic aneurysm was present in over half of the cases of aortitis in 1946. In 190 autopsies on neurosyphilitics 561 were found to be

G P I, 38 meningovascular, 5 pachymeningitis haemorrhagica and 3 transverse myelitis (in 48 there were insufficient data) The age at death for aortitis and neurosyphilis was about 40 years Neurosyphilis is quoted as constituting 0.4 per cent of all admissions to Mulago, which includes a Mental Hospital. Tabes is rare Microscopically the changes in neurosyphilis of the brain are the same as those seen in Europeans Ghomata are more frequent than intracranial gummata. In other tissues, diffuse syphilitic fibrosis and gummatous lymphadenitis were not observed

[The author strays far from his title and wanders upon rather uncertain territory]

C J Hackett

FISHER, A C, FISHER, MONICA M & LENDRUM, A C **Tropical Primary Phlebitis.**  
*J Path & Bact.* 1947, July, v 59, No 3, 405-15, 6 figs on 3 pls

This paper records a continuation of the studies first reported by FISHER [this *Bulletin*, 1942, v 39 199], and reference is made in it to the paper by MANSON-BAHR and CHARTERS [*ibid*, 1946, v 43, 1186] and to that by GELFAND [*ibid*, 1947, v 44, 539] The authors think that the conditions described by these other workers and themselves are the same Fisher writes from the Roan Antelope Hospital Service, Luanshya, Northern Rhodesia, Lendrum from the Department of Pathology the University and Western Infirmary, Glasgow

They have now seen 71 cases of tropical primary phlebitis (as they now name the disease), of these, 7 were fatal Two main types are defined phlebitis major (68 cases) in which large veins are involved, and in which there is a general reaction, with fever, and phlebitis minor, which is a lesion of small veins, easily diagnosed when the veins involved are superficial, in which general symptoms are slight In the severe form the onset is usually sudden, with local pain, tenderness and swelling over the affected vein, and muscular spasm There is venous engorgement distal to the inflamed area, and secondary thrombosis occurs In milder cases there is no residual oedema (after subsidence of the acute condition in 2-3 weeks) but in severe cases the limb may be left in a condition of permanent oedema The authors think that some of the cases of stiff neck reported by Manson-Bahr and Charters may have been due to deep-seated phlebitis No suppuration or embolus formation has been noticed

Of the 92 lesions reported, 34 were of the femoral vein, 8 of the popliteal, 16 of the axillary, and 7 of the subclavian vein, but other veins, including the internal (8) and external (6) jugular veins and the portal system (5), may also be involved The disease may be fatal when cerebral sinuses or important veins are diseased and since these veins may become involved after onset in a superficial vein, the prognosis should always be guarded

Sulphonamides were of no apparent benefit in treatment, but the use of anticoagulants would seem to be worth trial Illustrative cases are described

The second part of the paper is devoted to a discussion of the aetiology and pathology of the condition Blood culture was negative in 11 of the 12 cases in which it was tried in the other one *Streptococcus viridans* was isolated, but this is not thought to be a significant finding Kahn, Widal and Weil-Felix tests were not found to be relevant, malaria, the sickling trait and helminthic infection were not important There was slight leucocytosis with (sometimes) moderate relative lymphocytosis

Tissues were available for microscopic examination from several patients, and the jugular vein of one was examined in detail and under good conditions In this there was a remarkable disruption of the normal tissues of the media and intima, with newly formed capillaries set in a loose oedematous groundwork in which there were large cells of uncertain nature and neutrophils The endothelial cells showed evidence of urgent proliferation, there were other

large cells (reacting polyblasts) and in these there were cytoplasmic inclusion bodies which were clearly demonstrated when stained by the phloxin-tartrazine method (described by LAXDRUM on p. 369 of the same issue of the *Journal*). The point is made that fixation of tissues in formalin is rarely satisfactory for this purpose and that formal-sublimite (1 part commercial formalin to 9 parts saturated aqueous mercuric chloride) should be used for 10-14 days.

The detailed description of the lesions should be read in the original. The authors point out that they may be very localized, and consequently easily missed. The changes are quite unlike those associated with bacterial infection and the presence of inclusion bodies raises the question of virus infection though no virus has yet been recovered. This seems to be a newly discovered disease which occurs only sporadically in Rhodesia (though the outbreak described by Manson-Bahr and Charters elsewhere in East Africa was more in the form of an epidemic). It may be more widespread in Africa than is at present realized, and there may be cases in which obscure symptoms (for instance splenic softening or splenic abscess) are in fact due to the same cause. The method of spread is not known.

Charles H. Stocks

CHARTERS, L. D. & MANSON-BAHR, P. E. C. Symmetrical Gangrene in the African. [Correspondence.] *Brit Med J* 1948, Mar 13 520

GELFAND (see this *Bulletin* 1947 v 44 837) described 6 cases of symmetrical gangrene of the feet, in S. Rhodesia. Charters and Manson-Bahr suggest that the aetiology of this condition may have been similar to that of thrombophlebitis (see this *Bulletin* 1948, v 45, 1188). There is some similarity of early symptoms between Gelfand's cases and theirs, and gangrene due to arterial thrombosis was seen in two of their patients in whom the first signs were of phlebitis.

Charles H. Stocks

HARRIES, E. J. LEWIS, A. A. G. WARRING, J. W. B. & DOWLING, E. J. Melioidosis treated with Sulphonamides and Penicillin. *Lancet* 1948, Mar 6 363-4 3 figs.

The authors describe five cases of melioidosis which occurred in West African soldiers at various places between Freetown and Rangoon, Burma, during 1946. Two of the cases, in which there were multiple abscesses in the liver, spleen or lungs, proved fatal in spite of treatment of one patient with sulphathiazole and of the other with various sulphonamide drugs and penicillin. It is considered unlikely that cases with multiple abscesses in the internal organs will respond to any known form of treatment.

Of the other three cases one had superficial abscesses and two had infections involving the lungs. All recovered after combined treatment with sulphonamides and penicillin. It is known that *P. aethiops* is not sensitive to ordinary concentrations of penicillin, but the strain from one of the cases now reported was inhibited *in vitro* by 6.0 units per ml. The treatment now recommended is to give sulphamerazine 2 gm. every 4 hours for at least 10 days and to incise all accessible abscesses or to aspirate them and instil penicillin locally. Where there is a rise in agglutinin titre serum may be used.

The suggestion that colonial roughness is associated with melioidosis was supported by the observation that the strain from the three patients who recovered were noticeably less rough than the others.

The report also indicates that an agglutinin titre of 1:80 is likely to be significant and a titre of 1:160 almost certain diagnostic of melioidosis.

J. C. Crumckhorn

## ENTOMOLOGY AND INSECTICIDES GENERAL

MUESEBECK, C F W Common Names of Insects of Medical Importance approved by the American Association of Economic Entomologists *Mosquito News* 1947, June, v 7, No 2, 70-72

This is a short list of insects, classified in two forms 1 By the common names with the scientific names appended (e.g., American dog tick—*Dermacentor andersoni*), and 2 *Vice versa*

Its importance is that the names are approved, but some of them are only of local use For instance the "common malaria mosquito" is *A. quadrimaculatus* Charles Wilcocks

DUBIN I N, REESE, J D & SEAMANS, LOIS A Attempt to produce Protection against Mosquitoes by Active Immunization *J Immunology* 1948, Mar., v 58, No 3, 293-7 [13 refs]

In this experiment the attempt to protect rabbits against mosquitoes by vaccination with mosquito antigen proved unsuccessful Moreover, the rabbits so inoculated with a crude suspension of mosquitoes became sensitized to mosquito bites in contrast to the normal non-sensitive rabbits The sensitized rabbits showed large indurated reddened papules at the site of the bites These cutaneous reactions began in about 30 minutes and reached their maximum size at about 5 hours

Attempts at desensitization of the sensitive animals were unsuccessful under conditions of the present experiment Passive transfer of the sensitivity to normal animals was also tried but without success

LOCH H & ABONNENC E Sur *Anopheles nunez-tovari* et *A. pessoai* en Guyane française Table d'identification des *Nyssorhynchus guyanais* [*Anopheles nunez-tovari* and *A. pessoai* in French Guiana Key to the *Nyssorhynchus* of Guiana *Bull Soc Path Exot* 1947 v 40 Nos 11/12 457-62

MOSQUITO CONTROL Suva, Fiji Revised 1947 43 pp, 39 figs [11 refs]  
Training Manual, including Section on the Organization of the Filariasis Campaign in Fiji [AMOS, D W, Senior Mosquito Inspector]

This short pamphlet was written by a retired successful business man who became a Mosquito Inspector when manpower was short during the war, and who developed great interest in, and aptitude for, entomological work. It is written as a guide for field inspectors, the language is simple and clear, and there are many excellent line drawings of mosquito larvae and adults showing the important anatomical features The mosquitoes concerned are those found in Fiji

The pamphlet includes a key for the identification of larvae notes on adults and their habits (various species of *Aedes*, *Culex* and others are described) a section on mosquitoes as vectors of disease, and a section on filariasis in which the author gives his views on methods of control

The author has studied his material at first hand, and has consulted recognized authorities The pamphlet will undoubtedly be useful, and indeed, has already proved its value the comments of Dr McGusty and Dr Buchanan in their forewords leave no doubt on that point

Charles Wilcocks

FLOCH, H. & ARO NENC, E. Phlébotomes de l'Guyane française (XXII) Clé d'identification de 144 phlébotomes mâles du monde connu. [The Phlebotomus of French Guiana. (XXII) Key to 144 Male Phlebotomus of the Americas.] Institut Pasteur de la Guy. no 14. Territoire de l'Inini. Publication N° 161. 1947 Sept., 17 pp.

SMITH C. V. & GOODE, H. N. The Control of Chiggers in Woodland Plant. / *Econom. Entom.* 1947 Dec., 40 No. 6 790-43.

JAYEWICKREME, S. H. & NILES, W. J. Rearing of *Trombicula aculeatoris* Walch. *Nature* 1947 Oct., 3 578.

The authors describe with much useful detail, the method by which they have reared four generations of this mite.

They generally feed nymphs or adults on eggs of mosquitoes, but have seen them feed on small freshly-killed insects of several sorts. Eggs are laid in damp cellulose wadding. They hatch in ten to twelve days. The larvae are fed on white mice which must be immobilized until the larvae have attached themselves. The engorged larvae drop off from the third to the seventh day. [See also this *Bulletin* 1940, v 43, 1079.] P. 4 *Bulletin*

KOMLS G. M. *Ixodes radfordi*, a New Species of Tick from Rats in Eastern India (Acarina: Ixodidae). / *Parasitology* 1947 Dec. v 33 No. 4, 497-5, 1 fig.

WHEATON C. B. WHITE, W. C. & MISHKIN, V. S. Airplane Spraying with DDT for Control of Salt-Marsh Mosquito Larvae. *Wetlands News* 1947 Sept. v 7 No. 3 103-8.

"Large-scale applications of DDT sprays from airplanes as pre-larval treatments gave no control of salt-marsh mosquito larvae in 1945.

Direct application of DDT sprays by airplanes is a feasible method of controlling salt-marsh mosquito larvae. The treatments must be applied before pupation commences and sufficient material should be applied so that it penetrates the vegetation cover. A minimum effective dosage was 0.4 pound of DDT per acre. More satisfactory control was secured from the application of 0.4 pound of DDT per acre. At this dosage a sufficient amount of DDT to control later larvae penetrated all except the tallest and densest vegetation.

BERT D. H. D.D.T. in S.E.A.C. / *Rev. New Med. Serv.* 1947 July 33 No. 2, 197-200, 1 chart.

GUNTHER, F. A. Thermal Decomposition of DDT and Benzene Hexachloride Mixtures. / *Econom. Entom.* 1947 Dec., v 40 No. 6, 874-7 [10 cols.]

"Thus it becomes apparent that benzene hexachloride in any of the forms studied has a pronounced deleterious effect upon the thermal stability of DDT in admixture. In all probability the hexachloride preparations contained minute traces of iron or other catalyzing materials which lent this response. Benzene hexachloride and its alpha, beta, gamma, and delta isomers appear to be quite stable thermally to 120°C. even with added ferric iron in contradistinction to the behavior of DDT under similar experimental conditions.



## REPORTS, SURVEYS AND MISCELLANEOUS PAPERS

CONGO BELGE Rapport sur l'Hygiène Publique au Congo Belge pendant l'année 1946 [Report on the Public Health in the Belgian Congo during 1946] [LAMBRICHTS, G P] 202 mimeographed pp, 2 charts & 2 folding maps

This report, in addition to covering the medical activities of the Belgian Congo during the year 1946, contains some observations relating to 1945, as publication of the report for the latter year was delayed

Staff shortage was acute during 1946, since as many members as possible were allowed to take post-war leave, and replacements were difficult to obtain The report contains the usual detailed statistical account of the work of government, missionary and philanthropic bodies Comprehensive figures are given for the incidence of the common infectious diseases, and for attendances, treatments and epidemiological data In many cases, comparative figures are given for the preceding ten to fifteen years

The report contains a vast amount of informative matter, and gives a very full indication of the extent and nature of the medical problems encountered and of the facilities available for dealing with them

*H J O'D Burke-Gaffney*

BULL INST HYG MAROC 1945, v 5, 97-189, 9 charts Rapport sur l'activité des Services de la Direction de la Santé Publique et de la Famille pendant l'année 1945 [Public Health Activities during 1945 in Morocco]

The Directorate of Public Health of Morocco encountered special difficulties in 1945 More than half its personnel was engaged on war duties, unprecedented scarcity, due to deficient rain, coincided with a severe epidemic of relapsing fever which spread from Tunisia and Algeria. There was also an outbreak of typhus fever and small outbreaks of plague in the Casablanca region Mild smallpox was also prevalent throughout the territory Malaria, on the other hand, was less prevalent than usual, thanks to deficient rain

Temporary hospital accommodation had to be created The total number of hospital admissions was 96,084 "fevers" were responsible for 59.5 per cent of these admissions Among these there were 1,520 cases of relapsing fever, 149 typhus fever, 275 smallpox, and malaria 6,510 cases, mostly mild Malnutrition contributed to high case-mortality rates

The death rates for the year in the 18 municipalities were Mussulmans 36, Jews 19.8, Europeans 10 per thousand

Registered cases of smallpox numbered 2,618, of which 36 were among Europeans, vaccinations numbered 1,667,898 Diphtheria prevalence is decreasing, only 203 cases and 16 deaths were recorded There were 51,975 declared cases of amoebic dysentery and 4,175 cases of bacillary dysentery These figures give an exaggerated idea of the importance of the outbreak During 1945, the influx of very large numbers of ill-nourished destitute persons, many of whom were suffering from diarrhoea with blood and mucus, was on such a scale as to preclude the possibility of laboratory investigation in most cases

Before 1945, no large-scale epidemic of louse-borne relapsing fever had ever been experienced in Morocco Cases of the African (tick-borne) form of the disease are reported from time to time, chiefly in the region of Port-Lyautey The Health Service was alive to the dangers of the introduction of epidemic relapsing fever from Algeria, but, unfortunately, adequate supplies of DDT were not available till the end of July, when the epidemic was near its height The

first cases were recognized in January and the incidence curve rose steadily during the subsequent six months. For the country as a whole the acme of the epidemic was reached in the early weeks of 1948. In any given locality, however, the epidemic was not so long drawn out—it usually reached its height in 3 or 4 months and then rapidly subsided. (By August 1948 the disease had disappeared from Morocco.) During 1945 28,300 cases of relapsing fever were notified. The case-mortality rate varied from place to place and from season to season, between 1.8 and 8.9 per cent.

Typhus fever notifications were 8,168—the disease was widespread. The case-mortality rate for natives of Morocco 13.7 per cent., was higher than usual owing to the undernourished condition of the population at risk.

There were 828 cases of plague.

Norman White

DOCUMENT ALGERIEN. *Sér. Soc.* 1948, Sept. 15 No. 9 13 pp. L'œuvre de l'Institut Pasteur en Algérie [SERRANT, Ed., Director] [The Work of the Pasteur Institute in Algeria.]

A review of work undertaken since 1909

GUYANE FRANÇAISE. Rapport sur le fonctionnement technique de l'Institut Pasteur de la Guyane Française et du Territoire de l'Inini pendant l'année 1946 [FLOCH, H., Director]. Report of the Pasteur Institute of French Guiana and Inini for the Year 1946. Publication No 151 168 pp. 1947 Cayenn

The amount of work done by the Director of this Institute and his assistants during 1946 was remarkable both for scope and quantity, and in the Report a very detailed account is presented. The tables of pathological and other scientific examinations performed occupy some 20 pages, and include statements of organisms found or cultured and of insects and other creatures identified.

In section 4 there are essays, of different lengths, in which current medical problems are discussed—leprosy and its diagnosis and treatment, tuberculosis, venereal diseases, yaws, leishmaniasis, brucellosis, meningitis, beriberi (of which there was an outbreak in 1945), cancer, and other conditions. Malaria is discussed in the following section, and an account is given of a series of investigations on spleen rates (8-10 per cent.), parasite rates (5-40 per cent.) *P. falciparum* being by far the most common) and other lodgers. *Anopheles aquasalis* and *A. darlingi* are the most common anophelines, but only the latter has been found infected in nature though *A. aquasalis* can be infected experimentally. In this section also there is an account of the preparation of diphtheria antitoxin (Ramon) and its use in a small outbreak, a detailed statement of the leprosy position and the measures taken to deal with it, and statement of the examinations performed in relation to the dysenteries and diseases of the typhoid group.

Examination for intestinal parasites (especially for *Ascaris*, hookworm and *Trichuris*) blood-group work, veterinary work, botanical work and entomological work (reported in great detail) complete this section. The Report concludes with a statement of vaccines sera, etc., prepared and of vaccinations performed.

The Report is long and detailed, and there is some repetition—but within its limits (as the account of an institute dealing largely with infective or parasitic diseases) it gives a comprehensive picture of conditions in French Guiana.

Charles H. Wood



It is less a book for the lay worker than for the doctor and, in fact, a hope is expressed that it may be useful for those working for higher degrees in Tropical Medicine.

There is very little to criticize and much to praise. One would perhaps have liked a little stronger warning about the use of carbon tetrachloride. One will look for results of the sulphone drugs in leprosy as they begin to be used in South Africa. A résumé of the use of the antibiotics might be helpful.

There are very few misprints, but there are a few mis-spellings such as "Chrysopsis" "carbasone" for carbarsone, "pharynoderma" and "S stercorales".

The cure of the sick African is rightly stated to lie in the training of African doctors in their own country. But this will take a long time and the economic development of the continent is being so accelerated that less highly trained men may have to be used for generations. Let us hope that a worthy Native Medical School may before long be set up in the Rhodesias.

C. C. Chesterman

MITCHELL, John P. (C.B.E. M.D.). *Anatomy and Physiology and Causes of Disease*, 2nd Edition. pp. xvi+228 87 figs. & 2 diagrams. Baillière's Elementary Tropical Handbooks. 1948. London Baillière Tindall & Cox, 7 & 8 Henrietta Street Covent Garden, W.C.2. [3s.]

This is the second edition of one of the Elementary Tropical Handbooks for nurses and orderlies which are becoming as familiar in the tropics as the publisher's "Aids" series are in Britain.

The elementary principles of anatomy and physiology are simply stated and adequately illustrated under headings which correspond with the various systems of the body.

The knowledge thus imparted is reinforced in each chapter by the inclusion of suggestions for a series of simple demonstrations on the living subject, the cadaver or on available animals etc. The whole is related to clinical and ward work by the introduction of notes on the common diseases of the organs or themes described.

Thus, theory, demonstration and application go hand in hand throughout the book and the student is kept close to demonstrable facts and familiar realities.

In the pathological section one misses among the various causes of disease any reference to congenital conditions, degenerations and neoplasms (except under unknown causes). The life history of the malaria parasite needs bringing up to date and the rickettsias might find a humble place between the viruses and the bacteria in view of the prevalence of some sort of typhus fever in so many parts of the tropics.

The author wisely insists in his preface that this book is meant to be used by those who are receiving tuition. All those engaged in teaching will find it an invaluable aid.

The only mispelling noticed was *Onchocerca* for *Onchocerc* on p. 13 and so in the index. This edition contains new sections dealing with blood pressure shock and blood transfusion. Otherwise only minor changes have been made in the revised text.

C. C. Chesterman

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# TROPICAL DISEASES BULLETIN

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1948

[No 7

## THE CHEMOTHERAPY OF RICKETTSIAL INFECTIONS

By G M FINDLAY, C.B.E., M.D., D.Sc., F.R.C.P.

Before the War of 1939-1945 there was no known drug which had any effect on rickettsial infections. Now a number of compounds of widely different chemical constitution have been found to inhibit the growth of rickettsiae in chick embryos or to influence rickettsial disease in mice. Only *para*-aminobenzoic acid and chloromycetin are known to have an ameliorative action on rickettsial infections in man, but acridine derivatives, streptomycin, certain sulphonamide compounds and methylene blue all have a rickettsiacidal action in animals.

Not all species of rickettsiae are equally susceptible to rickettsiacidal agents. *Rickettsia burneti*, the causal agent of Q fever, for instance, is unaffected by penicillin or sulphonamides (SPICKNALL *et al* 1947).

There is still some doubt as to the best method of determining anti-rickettsial action. Three techniques are possible—(1) the injection of rickettsiae and drug into developing hens' eggs, (2) intranasal instillation of rickettsiae and intraperitoneal injection of the drug in mice counting the lung lesions, (3) intradermal inoculation into rabbits of a mixture of rickettsiae and drug after preliminary incubation. It is probable that, as in the case of malaria, each compound should be tested in more than one host, in this case in mice or rabbits and in the developing chick embryo.

In chemotherapeutic studies the following agents have been investigated—

### (i) *para*-Aminobenzoic Acid (PABA)

The effectiveness of *p*-aminobenzoic acid (PABA) in mice infected with murine typhus was first demonstrated by SNYDER *et al* (1942), they employed it on finding that sulphonamides appear to stimulate the growth of rickettsiae, since PABA is a known sulphonamide antagonist. Evidence of the action of PABA in a considerable number of rickettsial infections was subsequently obtained in many laboratories. In the yolk sac of developing chick embryos PABA or its sodium salt inhibits the multiplication of *Rickettsia mooseri* (GREIFF *et al* 1944, HAMILTON *et al* 1945), *R. prowazeki* (HAMILTON *et al* 1945, HAMILTON 1945) and *R. orientalis* (SNYDER *et al* 1947), *R. rickettsi* (HAMILTON 1945) the susceptibility of *R. quintana*, *R. burneti* and *R. akari* is not yet known. In experimental rickettsial infections the mortality in white mice (SNYDER *et al* 1942), gerbils (SNYDER and ZARAFONETIS 1945, MURRAY *et al* 1945, ZARAFONETIS *et al* 1946) cotton rats (SNYDER *et al* 1947), and guinea-pigs (ANIGSTEIN and BADER 1945, 1946), is considerably reduced by PABA. *Li*

In 1944 YEROMANS *et al.* obtained a favourable therapeutic effect in patients in the first week of epidemic typhus in Egypt. The figures obtained in this study have been examined statistically by SVYDER *et al.* (1947). 20 patients were treated with PABA and 19 alternate cases with those treated, were used as controls. Treated patients had shorter fever, fewer complications and a lower mortality rate than the untreated controls. These differences were significant. In the treated group, there was a significant correlation between the final score (the number of days of fever plus the number of complications) and the duration of the illness before therapy was instituted. SVYDER *et al.* (1947) also report the results of treating 60 patients suffering from typhus in the Dachau Concentration Camp in Germany in May 1945. Analysis of the results shows that there were statistically significant differences between PABA-treated and untreated patients as regards duration of fever, incidence of complications and mortality. All the evidence suggests that treatment begun early in the first week of illness is more effective than treatment begun late in the same week. In Northern Nigeria, during an epidemic of typhus, MONTGOMERY and BUDDEX (1947) treated six of the worst cases with PABA. All recovered whereas the mortality rate in the outbreak as a whole was 25 per cent.

SMITH (1946) reported the use of PABA in 29 cases of murine typhus. LEVY and AROLD (1946) in 6 and DIAZ RIVERA *et al.* (1946) in 4 cases, all with apparently good results. SMITH carefully compared his results with those in 29 controls. Of the treated cases only 7 had fever for 12 days or more whereas in 22 of 29 controls the temperature was above normal for at least 1 day. The average duration of fever in the two groups was 10.3 and 13.2 days respectively. DIAZ RIVERA *et al.* (1946) gave total doses 142 to 136 gm. a dose of 2 gm. in 25 ml. of 5 per cent. sodium bicarbonate solution was given every 4 hours. Subjective improvement began in from 4 to 48 hours after the beginning of treatment.

One patient suffering from Rocky Mountain spotted fever was successfully treated with PABA by ROSE *et al.* (1945). MALONEY *et al.* (1946) similarly treated one case. FLURY *et al.* (1946) obtained good results in nine out of ten patients. Blood levels of 30 to 60 mgm. per 100 ml. were necessary for success. TICHENOR *et al.* (1947) used PABA in 8 children suffering from Rocky Mountain spotted fever. All recovered but in the previous 36 patients who had not received specific treatment only 7 had died. The most striking result was in a patient who was given the drug on the third day of illness. The daily dose was 0.7 gm. per kilo of body weight in 24 hours divided into 3 hourly doses. RAVENEL (1947) reported five cases in children and adolescents from 3 to 17 years old. The following case is typical of those treated.—

A delirious wasted boy 17 years old suffered from a haemorrhagic rash together with conjunctivitis, palatal exanthema and scrotal oedema. *para*-aminobenzoic acid, 5 gm. in 5 ml. (a 5) 1% solution (sodium lauryl sulfate), was given orally every two hours for the first two days. At the end of this time the blood concentration of PABA was only 4 mgm. per 100 ml. The dose was then increased to 5 gm. every two hours in 50 ml. (solution). After 24 hours the blood level had risen to 18 mgm. and a day later to 32 mgm. per 100 ml. The temperature dropped sharply on the fifth day and was normal on the sixth when the rash faded rapidly, the mind cleared and the boy was almost well. The other four cases improved equally rapidly.

WILKS and BOCKHE (1946) in treating a girl aged 4½ years with PABA 2 gm. in 10 ml. of 5 per cent. sodium bicarbonate solution with 1 ml. of grape juice. This dose was repeated every 4 hours for 8 days. Grape juice helped the patient to retain the drug, which had previously been vomited.



Successful results in the treatment of 18 cases of scrub typhus were recorded from Burma by TIERNEY (1946)

There is now general agreement that, if success is to be obtained with PABA, certain conditions must be fulfilled. Good results from PABA therapy are to be expected in epidemic, murine and scrub typhus and the same is probably true of other forms of typhus, but only when treatment is begun during the first eight days of the disease. Thus, if there is clinical or epidemiological evidence to point to rickettsiae as the cause of a particular disease, it is as well to begin PABA treatment while waiting for the diagnosis to be established by laboratory tests, provided that certain contraindications are not present.

Precisely what is the optimum concentration of PABA in all rickettsial infections is at present unknown. Some of the PABA in the body is changed into *p*-aminohippuric acid, which is inert against *R. prowazeki*, *R. mooseri* and *R. orientalis* (SNYDER *et al* 1947) in experimental infections and probably against other rickettsial infections as well. Analyses made with Mirick's soil bacillus (MIRICK 1943) suggest that about 80 per cent of all diazotizable substances in the serum is free PABA when the total concentration in the serum is 15 to 20 mgm per 100 ml. In developing hens' eggs the minimum concentration of PABA required to achieve inhibition of multiplication is approximately 5 mgm per 100 ml for *R. prowazeki* and *R. mooseri*, but with *R. orientalis* it is at least 35 mgm per 100 ml. SNYDER *et al* (1947) therefore recommend that sufficient PABA should be given to attain promptly and to maintain for the entire period of the therapy a blood concentration, as free diazotizable substance measured against a standard of PABA, of 10 to 20 mgm per 100 ml for patients with typhus and of 35 to 40 mgm per 100 ml for patients with scrub typhus or Rocky Mountain spotted fever. Since PABA is rapidly excreted in the urine, the drug must be given at frequent, regular intervals during the day and night. The initial dose is roughly 0.05 gm per pound of body weight (0.11 gm per kilo) or 8 gm for a patient weighing 160 pounds (72.5 kgm). This is followed by a dose of 1 to 3 gm every two hours day and night throughout the course of treatment. The PABA administered should be chemically pure, odourless and almost colourless in powder form. In solution a faint brown colour is present. At least equimolar amounts of sodium bicarbonate should be given with each dose of the free acid (12.5 ml of a 5 per cent solution of sodium bicarbonate for each gramme of PABA). The amount of bicarbonate must be varied so as to keep the urine neutral or alkaline. For convenience, the powder (PABA) is mixed with a 5 per cent solution of sodium bicarbonate at the bedside immediately before each dose. After taking the dose the patient should be given 100 ml or more of water to drink.

SNYDER *et al* (1947) used a 10 per cent solution of the sodium salt of *p*-aminobenzoic acid, adjusted to a pH of 7.0, for the treatment of a patient with typhus contracted in the laboratory. A 10 per cent solution of the salt can be made up in bulk and stored in the cold for some days. No bicarbonate solution is necessary unless the urine becomes acid.

It is imperative to estimate the blood concentration at frequent intervals, particularly in patients with azotaemia and where appreciable fluctuations in fluid intake and urinary output occur from day to day. If possible, the blood concentration should be estimated every four hours during the first 24 hours, immediately before a dose of PABA. Except when renal insufficiency is present, estimations may then be limited to once in every twenty-four hours.

Intramuscular administration (the solution being sterilized by filtration through a Seitz filter) is unsatisfactory, but intravenous drip injection may be of value in patients who are unable to swallow. The rate of flow is adjusted to permit the infusion of from 25 to 30 gm of the drug in the course of 24 hours.

It is advisable to continue treatment for at least 48 hours after the temperature has become normal, otherwise both in typhus and scrub typhus the temperature may rise and in the latter condition the adenopathy may recur (TUNNEY 1946).

If the urine is acid there may be a precipitation of crystals of PABA in the kidney tubules. The pH of the urine should be tested with litmus paper at least twice daily as long as patients have measurable concentrations of the drug in the blood. Usually it is only in cases of azotaemia that more than 13 to 20 ml. of a 5 per cent. solution of sodium bicarbonate for each gramme of PABA is necessary to bring the pH of the urine to 7.0 or higher. Signs of renal involvement, such as azotaemia or haematuria, are less frequent and less severe in the treated than in untreated typhus patients. The urine of some patients under treatment with PABA contains reducing substance of unknown significance.

*p*-aminobenzoic acid is not without toxicity. In rats a single dose of 10 gm. per kilo of body weight kills 90 per cent. of immature and 45 per cent. of adult rats. The main pathological change found by ROBIN *et al.* (1947) was hyperaemia of the distal segment of the stomach. PABA added to the diet for 6 months to the extent of 4 per cent. produced no lesions in rats.

In patients, one of the main toxic symptoms is nausea with occasional vomiting. It is, however, rarely necessary to interrupt treatment for this cause and 250 gm have been given without evil effects. Leucopenia may be seen in some typhus patients treated with PABA. White cell counts should therefore be performed on every patient daily from the start of therapy until three or four days after its cessation. When the total white count falls below 3,000 per cmm. or the percentage of polymorphonuclear leucocytes below 45 per cent. no further treatment should be given. In each individual case however it is necessary to determine whether a falling leucocyte count is more serious than the withdrawal of the inhibiting effect of PABA on the rickettsiae.

There is some evidence that PABA slightly decreases the carbon dioxide combining power of the serum possibly also it slightly and transiently impairs liver function as shown by prothrombin and cephalin-flocculation tests.

If PABA crystals appear in the urine the administration of the drug should be stopped at once. In patients who are too weak to swallow properly care must be taken in giving PABA by mouth. Aspiration of PABA may be followed by severe tracheo-bronchitis. The presence of renal insufficiency before treatment or its appearance during the course of therapy is not a reason for withholding or discontinuing PABA, provided that the blood concentration is determined frequently that adjustments in dosage are made accordingly and that the urine is kept neutral or alkaline in reaction.

PABA therapy is probably not indicated for typhus patients under 40 years of age if they have been adequately vaccinated against the disease (ECHE *et al.* 1945) unless they show signs of developing a very severe infection. In cases of suspected scrub typhus PABA should be administered irrespective of any history of previous vaccination since there is as yet no satisfactory evidence that vaccines prepared from *R. orientalis* have any beneficial effect on the course of the disease in human beings.

SXTEDER *et al.* (1947) found no lesions which could be regarded as evidence of poisoning with the drug in four patients who died despite adequate doses of PABA. One fatal case showed an unexplained nephrosis. Possibly PABA might be more toxic in those with severely damaged livers.

Secondary bacterial infections are not uncommon in patients with typhus. The presence of such infections does not contraindicate PABA therapy but sulphonamides are contraindicated since their action is inhibited by PABA. They should therefore never be given during the acute febrile phase of a

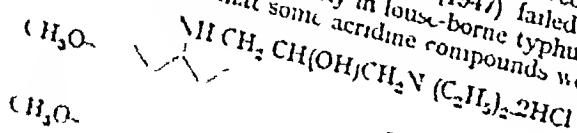
rickettsial disease under PABA treatment or while measurable amounts of PABA are still present in the blood. Penicillin is obviously the drug of choice where the secondary bacterial organisms are susceptible to it. Penicillin may be used to supplement, but not to replace, PABA.

In view of its use in rickettsial infections and also because of the relationship of this compound to sulphonamide action, the pharmacology of PABA has received considerable study. Earlier investigations are reviewed by LUSBACHER (1944). According to BLOOMBERG (1946), PABA is rapidly absorbed within 8 hours from the intestine, chiefly the small intestine, but only about 50 per cent of an oral dose is absorbed. LUSTIG *et al* (1944), using PABA in which the nitrogen was replaced by the isotope  $N^{15}$ , found that there was no utilization or storage of the labelled nitrogen. 82 per cent of the labelled compound was excreted 19 hours after an injection. When given by mouth PABA appears in the urine after 8 hours. Very little free PABA is present, most of it being converted to *p*-aminohippuric acid in the liver. Part of the *p*-aminohippuric acid is acetylated before excretion.

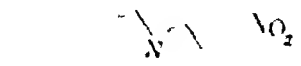
Very little is yet known of the mode of action of PABA on rickettsiae. However at least one variety of *Neurospora* is known which requires sulphamide for its growth. The growth-promoting action of sulphamamide is inhibited by PABA. LICO and SOLOMONS (1947) have shown that PABA inhibits the growth of *Bacterium coli*. GREIFF and PRICKERTON (1948) think that PABA acts by increasing the oxygen uptake of typhus-infected eggs. Ortho and meta-aminobenzoic acid are not rickettsiastatic and do not increase oxygen uptake. BENOVO (1947) believes that PABA depresses the body temperature so that rickettsiae cannot multiply. Methods of estimating *p*-aminobenzoic acid in the tissues have been devised by LEWIS (1942), KIRCH and BERGEM (1943) and PENNINGTON (1946). Microbiological assay is the simplest method, the organism used being either *Lactobacillus arabinosus* 175 or preferably, according to Pennington, *Leuconostoc mesenteroides*. The extent of growth after 15 hours at 37°C is determined turbidimetrically (THOMPSON *et al* 1943).

(ii) Acridine Compounds

Claims have been made that mepacrine is of value in the treatment of louse-borne typhus either when it is given alone (VAN MEERENDONK 1942a) or with cichium (VAN MEERENDONK 1942b). These results have not been generally substantiated though in murine typhus ARBOVA (1945) believed that mepacrine is beneficial. FERRO-LUZZI and FERRO-LUZZI (1947) failed to detect any good results from mepacrine intravenously in louse-borne typhus. During the war FUSSENGER (1945) found that some acridine compounds were effective in



(I)



(II)

2,3-dimethoxy-6-nitro-9-(diethylamino)propylamine hydrochloride. The most active of compounds were 2,3-dimethoxy-6-nitro-9-(diethylamino)propylamine hydrochloride and 2,3-dimethoxy-6-nitro-9-(diethylamino)propylamine hydrochloride.

arsenical salt of the former 1 molecule of nitroacridine being combined with 2 molecules of *p*-glycolyl aminophenylarsonic acid the arsenic being attached at nitrogen atoms (I) and (II). The previous information that rutinol is composed of two parts of nitroacridine with three parts of arsenic trioxide is incorrect.

No serious toxic manifestations attributable to these drugs were noted in a number of patients who received 2.5 gm. of nitroacridin 3582 or 4.0 gm. of rutinol given in divided doses over a period of two and a half days (FUSCHNER 1945 HOLLER and ZAJITSCHKE 1944 HOLLER 1944). The reported clinical effectiveness of these drugs in the treatment of epidemic typhus and trench fever (HOLLER and ZAJITSCHKE 1944 HOLLER 1944) requires further investigation.

SMADAL *et al* (1947a) confirmed the fact that nitroacridin 3582 and rutinol have a definite rickettsiastatic action on *Rickettsia prowazekii*, *R. mooseri*, *R. rickettsii* and *R. orientalis* in the developing chicken embryo. Acridine (*m*-8-diamino-10-methyl acridinium chloride) was active when the dose was 0.4 mgm. per egg, close to the toxic level. Mepacrine dihydrochloride in amounts up to 2.0 mgm. per egg had no effect on *R. prowazekii* or *R. rickettsii*. 4.0 mgm. doses killed all embryos.

A comparatively simple compound prepared by ALBERT *et al*. (1945) 2-nitro-5-amino-acridine was found to be effective in doses of 0.2 mgm. per egg. This dose is as effective as 0.4 mgm. of nitroacridin 3582, but the former is more toxic as 0.4 to 0.5 mgm. doses killed one-half to two-thirds of the embryos. Proflavine 2,8-diaminoacridine is without chemotherapeutic effect on rickettsiae.

There is no evidence that nitroacridin 3582 and *p*-aminobenzoic acid act synergistically on rickettsiae (SMADAL *et al*. 1947b). Nitroacridine is toxic to mice in doses of 200 mgm. per kilo of body weight when given subcutaneously and in doses of 25 mgm. per kilo of body weight after intravenous injection.

*The Mode of Action of Acridine Compounds*—Observations by McILWAIN (1941 and 1942) and MARTIN and FISHER (1944) show that the bacteriostatic properties of acridines such as acridine base and proflavine are inhibited by adenine-containing substances, adenine, adenylic acid, coenzyme and yeast nucleic acid, as well as by certain intermediate products of the action of these substances.

FITZGERALD and LEE (1946) have shown that several of these substances counteract the inhibition of growth of bacteriophage which is displayed by acridine compounds (FITZGERALD and HARRITT 1946). SMADAL *et al* (1947a) found that relatively large amounts of yeast nucleic acid were required to block the rickettsiastatic action of nitroacridin 3582, the ratio being 200 to 1 when as in the case of bacteriophage the ratio according to FITZGERALD and LEE (1946) was only 25 parts to 1 part of 2-amino-8-(*p*-aminophenyl) acridinium chloride. It seems probable that the mechanism of rickettsiastatic action by nitroacridin is one of interference with the adenine-containing compounds of the organism or host cell in a manner similar to that postulated for bacteriostats (McILWAIN 1941 and 1942 MARTIN and FISHER 1944). ANDREWS and KING (1946) suggest that acridines inhibit the process of rickettsial multiplication by interfering with the acidic phosphoric acid groups, which are salient features of nucleic acid and certain co-enzymes. In any case the mode of action of acridines is different from that of *p*-aminobenzoic acid. It may be noted that the minimal effective dose of nitroacridin 3582 in development, *Lens* injected with *A. mooseri* is slightly less than that of *p*-aminobenzoic acid though both are of the same magnitude. Thus 0.4 mgm per egg of nitroacridine produces decided inhibition while 0.5 mgm per egg of *p*-aminobenzoic acid is about the minimal effective dose (HAMILTON *et al*. 1945).

Nitroakridin 3582 has some action on the influenza virus and on viruses of the psittacosis-lymphogranuloma group. It is said to be active against haemolytic streptococci *in vivo* in a dilution of 1 in 250,000 and against staphylococci in 1 in 40,000.

### (iii) Antibiotics

GREIFF and PINKERTON (1944), GREIFF *et al* (1944) and MORAGUES *et al* (1944) found that penicillin in large doses had some inhibitory action on the growth of the rickettsiae of murine and epidemic typhus in mice, but against Rocky Mountain spotted fever it was useless (FITZPATRICK 1945). *In vivo*, however penicillin shows little activity, against either louse-borne typhus (YEOMANS *et al* 1944, VAN DEN ENDE *et al* 1946) or against scrub typhus (BLAKE *et al* 1945). Tyrothricin had no action in mice infected with murine or epidemic typhus (VAN DEN ENDE *et al* 1946). The effect of streptomycin on the growth of rickettsiae in eggs is more pronounced (MORGAN *et al* 1947, SMADEL *et al* 1947b and c). In addition to *R. prowazeki*, *R. mooseri* and *R. rickettsi*, *R. akari*, the newly recognized agent of rickettsialpox (HUEBNER *et al* 1946), is affected by doses as small as 1 mgm per egg. The administration of 10 mgm per egg resulted in a distinct lengthening of life of the infected embryos. Curiously enough, *R. orientalis* is scarcely affected by streptomycin. Streptomycin has been shown to have a curative action on *R. burneti* both in the infected hen's egg and in guinea-pigs (HUEBNER *et al* 1948). Dihydro-streptomycin (DONOVICK and RAKE 1947) has some general rickettsiastatic activity, but it is less than that of streptomycin. The action of streptomycin against rickettsiae is reduced by substances such as semicarbazide (RAKE and DONOVICK 1946) which also reduces the bactericidal action of antibiotics, thus suggesting that antibacterial and antirickettsial action go hand in hand.

Combined treatment of embryos infected with the four susceptible rickettsiae with 10 mgm of streptomycin and 0.5 mgm of *p*-aminobenzoic acid results in a more striking inhibition of growth than is obtained with similar amounts of either drug alone. In a like manner, 10 mgm of streptomycin and 0.4 mgm of nitroakridin display an additive effect in embryos infected with *R. mooseri* and *R. rickettsi*.

LIRLICH *et al* (1947) showed that a *Streptomyces* obtained from the soil of a field near Caracas, Venezuela produced an antibiotic chloromycetin which had a therapeutic effect on *R. prowazeki* in chick embryos. This was confirmed by SMADEL and JACKSON (1947) who found this antibiotic active in chick embryos against *R. prowazeki*, *R. mooseri* and *R. rickettsi* as well as in mice infected with 25 to 100 MLD of *R. orientalis*. In mice 0.1 to 1.5 mgm intraperitoneally or 1.5 to 5 mgm orally were required to cure infection. *R. akari* was also affected in mice and in embryonated eggs. Similar results were obtained in man by PINE *et al* (1948) working with epidemic typhus in Bolivia. Sixteen patients were treated either intravenously or by mouth for three days. Intravenously 10 mgm per kgm was given three times a day for three days while by mouth 15 mgm per kgm was administered without toxic effects. Three to four hours after intravenous injection there was improvement in headache, backache and vision while after oral medication good effects were noted six to eight hours after the first dose. There were no deaths. Similar doses were given to five normal controls without any toxic effects. Recent reports suggest that chloromycetin is of value in scrub typhus in man.

### (iv) Dyestuffs

Methylene blue was shown by OTTO and SCHÄFER (1936) to have an action on murine typhus infection in mice, a result confirmed by KIKUTHI and

SCHILLING (1944) in guinea-pigs. PETERSON (1944) used toluidine blue with some success in murine infections in mice.

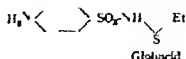
Later PETERSON and FOX (1944) and McLIMANS and GRANT (1944, 1945 and 1947) found that both toluidine blue and methylene blue were active against *R. orientalis* in mice, while AUGUSTIN and BADER (1945) obtained similar results in Rocky Mountain spotted fever. Both dyes are highly effective in mice in the oral maximum tolerated dose of 7.5 mgm. and in cotton rats against intraperitoneal injections of rickettsiae even when therapy is delayed until a systemic infection is well established. Methylene blue is also effective against intracerebral infections in mice, but when given subcutaneously the drug is much less active (PETERSON and FOX 1947). In mice methylene blue appears to be more effective than *p*-aminobenzoic acid against *R. orientalis*.

ANDREWS *et al.* (1946b) tested a number of dyes against rickettsiae injected intranasally into mice and intradermally into rabbits. The results of the two tests were in close agreement. The only dyes which showed any activity were methylene blue, toluidine blue, new methylene blue and 3-diethylamino-7-di-*n*-butylaminophenyl-thionium chloride hydrochloride among thiazines and a selocazine, selenium-methylene blue. Unfortunately the good results obtained in animals have not held good in man. STEARNS *et al.* (1946) found that methylene blue, largely owing to its toxicity was without effect in scrub typhus in man. It has been found that the rickettsiastatic action of methylene blue in mice infected with *R. orientalis* is greatly enhanced if the animals are placed in an atmosphere containing 50 per cent. of oxygen (McLIMANS and GRANT 1947). Unlike the acridines and *p*-aminobenzoic acid, toluidine blue and methylene blue are active against rickettsiae *in vitro*. Sodium nitroprusside reduces the acute toxicity of methylene blue (PETERSON *et al.* 1943) unfortunately it seems to have very little action on the chronic toxic effects of the drug (PETERSON and FOX 1947).

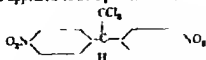
### ( ) Sulphonamide Derivatives

The commoner sulphonamides are without action on rickettsiae. In fact in experiments involving the adaptation of rickettsiae to mouse lung it is usual to give the mice sulphathiazole or sulphadiazine to protect them against secondary bacterial infections.

During the war it was found that some sulphonamides were however active against murine typhus in mice. Of these globocid was the most effective.



Another compound appeared to be equal to methylene blue in its action on



*R. mooseri*.

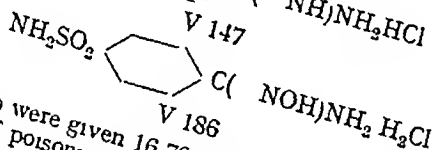
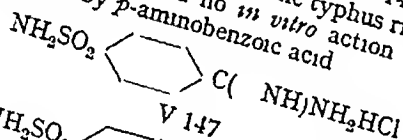
The most extensive series of sulphonamides however was that studied by ANDREWS *et al.* (1944) and VAN DEN ENDE *et al.* (1946) in mice inoculated intranasally with murine and epidemic typhus rickettsiae.

The compounds showed activity as follows —

No	Compound	A* mgm	B* mgm
V 147	<i>p</i> -Sulphonamidobenzamide hydrochloride	24	4
V 186	<i>p</i> -Sulphonamidobenzamide hydrochloride (free base of V 186)	24	2
V 207	<i>p</i> -Sulphonamidobenzamide hydrochloride	16	4
V 192	<i>p</i> -Sulphonamethylamidobenzamide hydrochloride	16	8
V 262	<i>p</i> -Sulphonhydroxylamidobenzamide hydrochloride	16	4
V 279	<i>p</i> -Sulphonamido- <i>m</i> -tolamidamide hydrochloride	16	>8
V 276	<i>p</i> -Sulphonamido- <i>m</i> -tolamidamide methyl ether hydrochloride	8	>4
V 231	<i>p</i> -Sulphonamidobenzamide ureide	16	8
V 232	<i>p</i> -Sulphonamidobenzamide ethyl ether hydrochloride	8	4
V 280	NN'-Dipropoxybenzamide- <i>p</i> -sulphonamide	16	8
V 281	NN'-Dimethoxybenzamide- <i>p</i> -sulphonamide	8	8
V 283	NN'-Diethoxybenzamide- <i>p</i> -sulphonamide	8	>8
V 238	<i>p</i> -Sulphonamidobenzamide ureide	8	2

A\* = Max tolerated dose for 15 gm mouse  
B\* = Minimal effective (wholly suppressive) dose given twice daily

All the hydrochlorides in this series were readily soluble in water the free bases were only sparingly soluble. The only compounds having a favourable ratio between toxicity and activity in mice were V 147 and V 186 neither protected guinea pigs from fever when epidemic typhus rickettsiae were injected intraperitoneally. These drugs had no *in vitro* action on rickettsiae their activity was not abolished by *p*-aminobenzoic acid



Two volunteers who were given 16.79 and 20.38 mgm of V 186 in six days showed no evidence of poisoning. In animals, there was a tendency for the blood pressure to be lowered and the blood urea to be raised. When V 147 and V 186 were tested in patients with epidemic typhus in North Africa and Naples the results were disappointing. The human kidney appears to be extremely susceptible to the action of the drugs. Severe degenerative changes were found in the renal tubular epithelium of fatal treated cases in Naples and a number of unexplained cases of vascular collapse made it inadvisable to increase the dose. The relation between chemotherapeutic action and chemical constitution in this group of compounds is discussed by ANDREWES *et al* (1946a). It is possible that these amidines and amidoximes enter the cell and are built up while nucleic acid synthesis is active, into some essential vital structure of the rickettsiae. It is obvious that only very slight modifications of the *p*-sulphonamidobenzamide molecule are needed to abolish rickettsiastatic action altogether. Many other sulphonamides and sulphones were devoid of action in mice inoculated intranasally. It must however be noted that this method of inoculation fails to demonstrate the protective action of *p*-aminobenzoic acid in mice.





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infection is commonly spread to the multi-mammate mice (*Mastomys*) which make use of gerbil burrows and pick up the fleas (*Xenopsylla eridos*). These mice also approach human habitations and transfer the infection to domestic rodents, whose fleas (*X. brasiliensis*) are effective vectors to man.

TOMIC (p 996) has failed to find infection in a small number of rodents examined in the Suez Canal Zone, there is no definite evidence that sylvatic plague exists there.

RAO (p 816) found that field rats near a village in India where plague was endemic were very susceptible to the disease, and he therefore argues that they have not been in frequent contact with the disease, and cannot be the cause of the endemicity in that area. It therefore seems a waste to fumigate rat holes in the fields, and attention should be concentrated on the more resistant rats of the village itself.

MACCHIAVELLO (p 519) reports a focus of sylvatic plague on the borders of Peru and Ecuador.

MIYARA and his colleagues (p 815) describe the very great epizootic of plague which exists in the wild rodents of Argentina and several outbreaks which have occurred in man, largely as a result of handling dead rodents. Pneumonic plague has occurred, which is difficult to diagnose and which spreads from man to man. Prevention entails education in the danger of handling wild rodents, and isolation of the patients in hospital. Sera and vaccines are not regarded as useful, and anti-rat measures, essential for towns, are not applicable to the conditions of sylvatic plague.

HUMPHREYS and CAMPBELL (p 758), as a result of surveys made in Canada, point out that plague is well established in ground-squirrels in parts of Alberta and Saskatchewan. So long as it is confined to these squirrels there is not much danger to man, but if rats invade the area and become infected, the problem will be serious. Rats are well established in the towns.

WAYSON (p 899) discusses the results achieved in field surveys in the United States during 10 years, when enormous numbers of rodents and fleas were examined. One infective flea can infect a series of animals. There is no evidence that rodent carriers of subacute or chronic plague are a factor in perpetuating the disease from one season to another but it seems likely that some form of recrudescence in the carrier of quiescent disease is necessary for carry-over by infection of fleas. PRINCE and WAYSON (p 816) have shown that a flea can remain alive and infected with plague in a virulent form for a period of 4 months in the nest of a hibernating squirrel but most of the fleas which were infected and remained alive did not retain the infection for the entire 4 months. The same authors (p 1064) show that a squirrel in whose skin plague is introduced while the animal is in hibernation in October may awaken 4 months later and subsequently develop acute manifestations of the local lesion, and lethal bacteraemia. A flea infected in October and placed on a healthy hibernating squirrel can retain the infection and transmit it during the following March.

Although at one time it was assumed that fasting fleas could not live longer than one month, and therefore that a voyage lasting 80 days ruled out the possibility of introduction of plague by fleas alone, MACCHIAVELLO (p 997) has shown that fleas taken alive in jute bags imported into Peru from India were capable of inducing plague by bite, although there was no possibility that the fleas could have received their infection during the voyage.

PERRY (p 76) and LAURIE (p 76) have written on the reproduction of the brown rat and the house mouse respectively. The papers are technical and detailed but have a bearing on studies of the rodent hosts of plague and indicate some of the mistakes that can be made if the subject is not studied with some care.

### Etiology

GIRARD (p. 520) indicates the importance of distinguishing between *P. pestis* and the pneumococcus in the diagnosis of plague pneumonia. Cultures should therefore be incubated at 20-28°C., not at 35°-37°C. and for inoculation or scarification tests, guinea-pigs rather than mice should be used since the latter are very susceptible to the pneumococcus. This organism may exert an antibiotoxic action on *P. pestis* and may prolong the incubation period to 10 days in primary plague pneumonia. In Madagascar the authorities have fixed a limit of 10 days for quarantine of contacts.

LAZARUS and GUNNISON (p. 1064) show that differentiation between *P. pestis* and *P. pseudotuberculosis* by phage action is not reliable. They also found that *P. pestis* phage acted on some strains of *Salmonella* and *Shigella*.

GIRARD and SANDOR (p. 800) have studied the toxin of *P. pestis*, a protein which may be injected as whole bacilli, or as a solution since it diffuses into liquid culture media. It is not an exotoxin. RAMON *et al.* (p. 800) show that plague toxin differs from true exotoxins in that certain antibiotic substances do not act on it.

### Clinical Findings and Treatment

Although meningitis is not regarded as one of the common lesions in plague, LAYDSBOROUGH and TUXFELL (p. 418) report 8 cases, all fatal, in a total of 203 cases. *P. pestis* was found in the spinal fluid in 5. In one the meningitis appeared to be primary but in the remainder it was a sequel of bubonic disease.

SORHEY and WAGLE (p. 418) discuss the treatment of septicaemic plague noting that septicaemia is the most important single factor determining death or recovery. They found that sulphadiazine (4 gm. followed by 2 gm. every 4 hours for not more than 10 days) gave the best results, reducing case mortality from 91 per cent. in controls treated with intravenous iodine to 31.9 per cent. Sulphathiazole was not so useful. The authors treated 1,604 patients in all.

SINGH and CHATRE (p. 77) found sulphadiazine more effective than sulphathiazole in the treatment of bubonic plague in India.

HOANG and CMO (p. 419) note that plague bacteraemia is readily controlled by sulphonamides, especially sulphadiazine, but that viable bacteria remain unaffected within buboes and may cause relapse.

MAGROU (p. 417) reports an outbreak of plague at Ferryville Tunisia, in which there were 37 cases and 10 deaths. Only 2 deaths occurred in the 28 who were treated with sulphadiazine. The Girard live vaccine was given to 60,000 people.

ROUX and MERCIER (p. 207) report that three of five patients with pneumonic plague were cured by administration of 65-75 gm. sulphathiazole. This is a striking result.

ALBERTO VIDELA (p. 659) has treated several cases of plague with sulphonamides and streptomycin. In one with signs of meningitis, intrathecal administration of streptomycin was followed by striking improvement. HERRLIER (p. 713) shows that streptomycin kills *P. pestis* in culture and is an effective treatment (more so than sulphathiazole) in mice and guinea-pigs infected with plague.

### Vaccination Control

BAKER *et al.* (p. 712) have investigated the antigenic structure of *P. pestis*. Various fractions were isolated, one of which, a carbohydrate-protein fraction, is probably the normal antigen of the intact cell, and is an envelope antigen. For vaccines all the antigens should be included.

MEYER (p. 816) sums up the measures taken to control plague. Recent work indicates that success in vaccination depends rather upon the actual mass of

bacterial protein injected than on the method of preparing the dead antigens, and that organisms grown on agar and killed by formalin are effective if enough are injected and if frequent "booster" doses are given. Urban plague, except in a few areas, is no longer a major problem, but sylvatic plague may be so. It is not known why human cases are so rare, although rodent plague is so very common, in the 14 States of the U.S.A. which are affected.

WAYSON *et al* (p 419) give the results of experiments with guineapigs which indicate that plague vaccines prepared from organisms grown at 39°C and killed by phenol or formalin, are effective in preventing death of the animals. In a city of 110,000 inhabitants, in India, SIMEONS and CHHATRE (p 77), inoculated 90,000 with a single dose of killed plague vaccine (Haffkine), in the face of an epidemic. The results were disappointing, and the authors conclude that it would be dangerous to rely on vaccination of this type, given as a single dose, and that the use of cyanogas, rat-bait and anti-flea measures is much more valuable.

The Indian Research Fund Association report on plague (p 997) shows that plague vaccine (either casein hydrolysate or agar vaccine) deteriorates if kept at 37°C, but not nearly so much at 0°C.

GRASSET (p 419) shows that a live avirulent plague vaccine has been largely used in South Africa, and that in 24,000 persons inoculated with it, there occurred only 15 cases of plague. The vaccine can be dried at low temperatures and kept for 2 years with little loss of antigenic power. Sylvatic plague is a very great problem in South Africa.

MACCHIAVELLO (p 78) and his colleagues (p 713) describe the use of DDT and of the rat poison sodium fluoracetate ( $\text{NaFAC}$ ) in stopping an epidemic of plague in a city in Peru where most of the rats were *R. rattus alexandrinus* and most of the fleas were *X. cheopis*. DDT as a 10 per cent powder was applied to the floors of all houses and left unswept for a week and elsewhere in likely rat harbourages. Sodium fluoracetate was incorporated in bait and placed with care out of reach of children. These measures were most successful. The author notes that 10 per cent DDT is toxic for rats (which lick their fur), and that sodium fluoracetate is toxic for fleas which suck the blood of poisoned rats. ELISHEWITZ (p 1064) advises that places frequented by rats should be dusted with DDT, to kill fleas and their larvae, and that alpha-naphthyl thiourea (ANTU) or sodium fluoracetate should be used for the rats, but with care and by skilled operators only. DDT and the modern repellents can be used in clothing, for the protection of field workers. GOUCK (p 78) has found 10 per cent DDT in pyrophenylite successful against fleas on rats, when it is dusted in their holes and burrows.

Reporting an outbreak of plague in Algeria, which was not pneumonic and in which no rats could be found, either alive or dead, GRENOILLEAU (p 658) suggests that the disease was probably transmitted from man to man by *Pulex irritans*. Control action in such an outbreak comprises prompt detection and isolation of cases, disinsection of patients and contacts, and daily medical supervision of contacts, as well as the other usual methods. The flea *Synosternus pallidus* may be a vector of plague in Dakar, and KARTMAN (p 420) has shown that DDT, either as a solution or as a dusting powder, is effective against this flea, when applied in huts.

Charles Wilcocks

## RABIES

OTTEN L. Investigations into Rabies. II. *Antonie van Leeuwenhoek J Microbiol. & Serol.* 1947 v 13, Nos. 2/4 101-27 1 fig. (21 refs.)

In this posthumous contribution of the late Prof. OTTEN detailed reference is made to the statistical and experimental work on rabies carried out by his deceased wife Maria J. OTTEN-VAN STOCKUM at the Pasteur Institute, Bandoeng, Netherlands East Indies.

The following paragraphs summarize the more important conclusions reached during a prolonged period of research —

The rate of mortality from rabies during or after treatment provides no reliable index of any particular treatment's efficacy: the sole criterion in this respect being a reduction in the occurrence of "failures" defined as cases in which symptoms appear more than 30 days after treatment has begun.

Monkey brain furnishes a more active antigen than rabbit or sheep brain and in anti-rabies immunization the superiority of monkey brain fixed virus (both living and formalized) over other vaccines is evidenced by the subjoined comparative results —

Method of treatment and when practiced	No. of persons treated	No. of deaths	Percent mortality	No. of failures	Percent failures
Pasteur method (1893-1905)	1421	9	0.63	7	77.7
Hogyes method (1906-1916)	1610	4	0.25	1	3.0
Monkey brain F.V. (living and dead) (1916-1940)	2919	2	0.07	0	0.0

At Bandoeng during a 25 years period there was no "failure" among persons treated in the first week after the bite whether with living (1916-32) or with killed, formalized (1933-40) monkey brain F.V. The vaccine most recently employed derives from a 10 per cent suspension of monkey brain in a 1.5 per 1000 concentration of formalin, heated for 5 days at 37°C. Prior to its administration it is diluted to 2 per cent, and the total quantity injected, over a 14 or 21-day period, is 1120-1,520 mgm., as against 470 mgm. of the living virus vaccine previously in use.

Two weeks' treatment was found to be as effective as a 3 weeks' course when judged by the failure rate and the rabicidal antibody content of vaccinated persons sera.

The fact that the average period of incubation in cases of rabies treated with formalized vaccine shows a definite shortening when compared with those treated with live vaccine not only disproves the statement of NICHOLSON (*Cent. J. Bact.* L. (b), Orig., 1946, 4, 647-775) and of PROCA and BUSTI (*this Bulletin* 1940 v 37 618) that the shortening is to be ascribed to the action of living F.V. but also encourages the hope that by the use of formalized vaccine the immunization process will attain its maximum more rapidly — within the first 30 days following the commencement of treatment — within the defined failure limit — and effect greater reduction in mortality.

Formalized vaccine when prepared as a 2 per cent suspension and kept at room temperature rapidly lost potency; stored as a 10 per cent suspension at 5°C, however it showed no appreciable decrease in activity. Deconcentration

of treatment is thus possible if the original 10 per cent suspension, preserved regionally under adequate storage conditions, is diluted to 2 per cent immediately before its administration

The testing of a 10 per cent suspension before and after centrifuging showed that both in virulence and antigenic activity the supernatant fluid was much inferior to the ordinary suspension and to the deposit

An experiment devised to ascertain whether, over a 14-day period, the immunization of the rabbit and the guinea-pig (in a total dosage of 20 mgm and 10 mgm respectively) could better be effected by consecutive daily injections of slowly increasing strength or by three adequately interspaced injections of increasing strength failed to show any difference in favour of the daily injection

IRR, G La prophylaxie de la rage Police sanitaire et vaccination preventive [Prophylaxis against Rabies. Sanitary Control and Preventive Inoculation] *Cahiers Méd Union Française Algiers* 1947, Oct, v 2, No 13, 615-31 [12 refs] G Stuart

The author deplores the comparative failure in France and in French North Africa of the sanitary regulations prescribed for the prevention and control of rabies. He attributes this failure, not to the inadequacy of the regulations themselves but to the fact that the requisite powers of enforcement are vested in local rather than in central authority. He compares the state of affairs in France unfavourably with that in Great Britain, where similar legislative measures have been enforced by central authority (the Ministry of Agriculture) since 1899.

In discussing the actual measures to be adopted the author urges large scale vaccination of dogs—free of charge to the owners—and goes so far as to state that vaccinated dogs are no longer susceptible to rabies.

He proposes the adoption of a specific programme for Algeria and includes therein a suggestion whereby the practice of vaccination may be stimulated *viz*, a relaxation in the case of vaccinated dogs of sanctions otherwise immediately imposed by the law. Thus a vaccinated dog having been in contact with an animal suspected of rabies would be subject to surveillance at home instead of to summary destruction. (Such leniency contrasts sharply with the measure in force which prohibits dogs from appearing on public thoroughfares unless muzzled and on the leash.) He further recommends that dog shows should be open only to those animals vaccinated against rabies.

Other measures in common practice elsewhere are also dealt with in the paper: the impounding and destruction of all stray dogs, the compulsory wearing of collars with ownership clearly indicated.

The author feels confident that the adoption of such a programme, coupled with the transfer of overall powers of enforcement from the communes to the prefectures would materially improve the far from satisfactory rabies situation existing in Algeria today.

REMLINGER P & BAILLY, J La rabia del lobo Criterio de la vacunación pasteuriana [Wolf Rabies and the Assessment of Pasteurian Vaccination] *Med Colonial Madrid* 1948 Mar 1 v 11 No 3, 115-18 G Stuart

## MALARIA

PRILIOCIOTTA R. Note sulla morbidità malarica nella zona Dire-Dana-Erer dell'Etiopia. [A Note on Malaria Morbidity in the Dire-Dana-Erer Area of Ethiopia.] *Atti Med. Italiana*, 1948 Jan. v 3 Supp. No. 1 25-8.

The English summary appended to the paper is as follows —

"The author has studied the malaria morbidity in the region of Dire-Dana-Erer in Ethiopia, observing in many subjects, many of them without temperature presence of many malaria parasites in the blood.

"He calls attention to the high endemicity of the malarial infection in that region."

DALAL, P. A. Bombay and its Malaria. *Indian J. Med. Sci.* 1947 Dec. v 1 No. 6 775-81 [11 refs.]

In this lecture the author refers to the outstanding epidemics of malaria that have afflicted Bombay City in the past to the numerous surveys and special investigations that have shown how the disease might be controlled, or even eradicated, at no prohibitive cost and the failure of the authorities to take effective steps to that end. No new facts are adduced but information regarding the local habits of the only vector *A. stephensi* is well summarized.

Norman White

ESTELA CASTELO Mammel A. Encuesta malarica de reconocimiento del Valle de Cañete. [Malaria Survey of the Cañete Valley.] Publicaciones de la Dirección General de Salud Pública, Departamento de Malaria. 88 pp 2 maps, 4 charts & 8 plans. [14 refs.] 1947 Feb. Lima, Peru.

The Cañete Valley is the southern part of the Province of the same name which forms the south-eastern part of the Department of Lima. The Valley covers an area of 21,800 hectares. Its mean altitude is 98 metres above sea level. Its estimated population is 31,710. The Valley watered by the River Cañete has a maximum width of 20 km. elsewhere its width varies from 13 to 17 km. It is very fertile. The geography, hydrography, geology and agriculture of the Valley are outlined and information is given about the social and economic conditions of the population. Pneumonias, pulmonary tuberculosis and enteritis are responsible for most deaths. Deaths attributed to malaria have declined markedly during the last decade. The malaria death rate in 1944 was 1.49 per thousand (49.32 per thousand all causes). 3,818 cases of malaria were reported with 18 deaths. Malaria is most prevalent during the first seven months of the year.

In November and December 1945 2,210 children below the age of 11 were examined. 295 (13.3 per cent) had enlargement of the spleen. In 101 of these the spleen was palpable only on deep inspiration. In 117 others it did not extend beyond the costal margin. In 20 the spleen reached the umbilicus.

The blood of 2,167 of these children was examined. parasites were found in 107 (4.9 per cent.). The percentage incidence of parasitic species was *P. vi* 54%, *P. falc. par.* 34.4 and *P. malariae* 11.4.

Only two species of *Anopheles* were found *A. punct. p. neipponi* and *A. punctimans*. The former is the chief vector of malaria. It is widespread, markedly anthropophilic and frequents human habitations. *A. p. neipponi* was only rarely found breeding and only occasionally captured in dwelling houses. It too shows a predilection for human blood but its role as a malaria vector has yet to be defined.

Norman White



KETTLE, D S & SELICK, G The Duration of the Egg Stage in the Races of *Anopheles maculipennis* Meigen (Diptera, Culicidae) *J Animal Ecology* 1947, May, v 16, No 1, 38-43, 2 figs [12 refs]

Wild-caught females of various races of *Anopheles maculipennis* were allowed to oviposit in small cages and the times of hatching of the eggs were observed. The data presented in this paper were collected in Italy in the spring of 1945 and analysis shows that at 10°C eggs of *A m maculipennis* develop more rapidly than do the eggs of either *A m labranchiae* or *A m melanoon*, but the difference becomes less at higher temperatures until at about 20°C it is negligible. The following examples are extracted from a table of mean incubation periods: eggs of *A m maculipennis* 10 days at 10.6°C and 4 days at 16.5°C, eggs of *A m labranchiae*, 12.6 days at 10.6°C, 4.2 days at 17.3°C, eggs of *A m melanoon*, 12 days at 10.8°C and 4.5 days at 17.0°C. The authors suggest that the quicker development of the eggs of *A m maculipennis* at the lower temperatures is possibly an adaptation to the more rigorous climate to which this race is exposed in its natural habitat as compared with that of the other races.

KARTMAN L, NEWCOMB E H, CAMPAU E J & MORRISON F D Mosquitoes collected in Dakar, French West Africa, incidental to Army Malaria Surveys *Mosquito News* 1947 Sept v 7 No 3 110-15

WHITE, R Senior An Analysis of a Series of Night Catches of *Anopheles* *J Malaria Inst of India* 1946 Dec, v 6, No 4, 417-23

These catches of anophelines were made in 5 localities outside the control area of the Korea Coalfield in the Hazaribagh Ranges in Central India. The catches were made for the first twenty minutes of each hour from 11.0 p.m. till daylight six times a month for 21 months.

Eleven species were obtained, but only three were collected in sufficient numbers to merit tabulation: *A culicifacies*, *A fluviatilis* and *A subpictus*. *A culicifacies* shows maxima in May, August and October. Hourly incidence decreased steadily from 23.00 to 5.00 hours and was followed by the usual increased entrance before dawn.

Captures of *A fluviatilis* were almost confined to October and November, when they represented 92 per cent of the year's total. Prevalence of this species was highest before midnight and decreased till the pre dawn entrance. Dissections have hitherto incriminated only *A fluviatilis* as a vector of malaria in this part of India. Malaria transmission however is active between July and September when this species is all but absent. *A culicifacies* is probably responsible for this in spite of the failure of dissections to confirm it.

REID, J A Type Specimens of Culicidae described by Laveran (Diptera, Culicidae) *Proc Roy Entom Soc of London* Ser B Taxonomy 1947, Aug 15 v 16 Pts 7/8, 86-91 [12 refs]

The author has been able to examine the original type specimens of six species of mosquitoes (two from Oceania and four from Indo-China) described by Laveran in 1901-1902. Perhaps the most interesting discovery relates to the identity of *Anopheles farauti*, a member of the *p. inclutus* group occurring in the New Hebrides. Examination of Laveran's original material shows that *A farauti* is defined by Knight and other recent American authors is identical with Laveran's original material. For this information all students of this difficult group will be grateful.

MACKERRAS M. J. & ROBERTS F. H. S. Experimental Malarial Infections in Australasian Anophelines. *Ann. Trop. Med. & Parasit.* 1947 Dec., v 41 No. 3/4 329-56 9 graphs. [74 refs.]

This investigation was undertaken in 1943 at Cairns, North Queensland, for the purely practical purpose of discovering the most useful mosquito to employ in the laboratory study of malaria transmission. The breeding and infecting of anophelines was done on a very large scale—233 000 engorged mosquitoes were used, 38,000 dissections were performed and 20 000 infected bites were inflicted. Seven species were from Queensland, *Anopheles punctulatus farauti*, *A. annulipes*, *A. amictus amictus*, *A. amictus hilli*, *A. merusensis*, *A. bancrofti bancrofti* and *A. stigmaticus* two were from New Guinea, *A. punctulatus punctulatus* and *A. longirostris*. A colony of *A. p. punctulatus* was eventually established, as supplies of the other species became insufficient—this colony flourished successfully until the work ceased in 1948.

The techniques of collecting, rearing, feeding and infecting the mosquitoes are described. The characteristics which influence an anopheline mosquito in malaria transmission were studied. One of these abundance was satisfied in the laboratory by *A. p. punctulatus* as it colonized so readily that adequate numbers were always available. All species would feed on man, but *A. p. punctulatus* was more avid for human blood than the others. *A. stigmaticus* and *A. longirostris* would feed only with reluctance. The authors regard longevity as a most important factor in laboratory work, perhaps even more so than willingness to feed. *A. p. punctulatus* was the longest lived species—it needed a humid atmosphere and a temperature about 70° to 75° F (21° to 24°C.) and not less than 6 cubic inches of space per mosquito. It needed also freedom from disturbance for it was found that overcrowding and frequent handling of the cages shortened life by keeping the insects in a state of abnormal activity. The two rare species *A. longirostris* and *A. stigmaticus* showed evidence of insusceptibility to infection. All the common species were highly susceptible though there were, of course individual variations in all species.

Finally a most careful study of *A. p. punctulatus* showed that this species was the most useful in transmission experiments, in all respects. There was however no marked difference between *A. p. farauti* and *A. p. punctulatus* in the laboratory studies, though the former is an important natural vector while the latter is not.

H. S. L arson

STACE, H. H. & GILLETTE H. P. S. Observations on Mosquitoes and Malaria Control in the Caribbean Area. Part III—Trinidad. *Mosquito News*. 1947 Dec. v 7 No. 4 157-9 2 figs.

Fifteen species of *Anopheles* are known to occur in Trinidad and Tobago of which the following five species are common—*A. aquasalis* the most important malaria vector, *A. bellator* an important vector in the heavy rainfall zones, *A. maculipalpus* and *A. allatipes* both suspected as minor carriers and *A. costalis* a zoophilic species.

Catches in Shannon down traps have proved that *A. aquasalis* has migrated inland over rough country as far as five miles from its salt marsh breeding places.

In the cacao estates tall shade trees called umbrellals (*Erythrina* spp.) are interplanted. These immortelles support a considerable flora of epiphytes of which the bromeliads are most numerous. The common bromeliad (*Guzmania sp.*) breeds enormous numbers of *A. bellator*.

The difference between the leaves of bromeliads, cacao and umbrellals has made it possible to use several chemical wears as bromeliacide. But results

have been obtained with 0.5 per cent copper sulphate and plans have been made to replace the immortelles with other trees as wind breaks, so that with the eradication of the breeding places of *A. bellator* endemic bromeliad malaria should disappear from Trinidad

H S Leeson

GABALDON, A. & COVA-GARCIA P. Zoogeografia de los anofelinos en Venezuela I Los dos vectores principales [Principal Anopheline Vectors in Venezuela.] *Tyrolasos sobre Malaria* Venezuela 1946 Mar, v 10 No 1, 19-32, 4 figs [25 refs]

Geographical distribution of *A. albimanus* and *A. darlingi* in Venezuela

KIVITS, M. Infection malarienne à *Pl. vivax* [Relapsing *P. vivax* Malaria] *Ann Soc Belge de Méd Trop* 1947, Sept 30, v 27, No 3, 333-5

The author returned on leave from the Belgian Congo in September 1946, after 8 years' continuous residence during that time he took daily prophylactic quinine regularly (0.3 to 0.4 gm). He had occasional light attacks of malaria

On his arrival on leave, on September 15, he had completed a suppressive course of quinine (1 gm daily for 15 days). At the end of September he had a typical tertian ague, which was treated with quinine (0.25 gm three times the first day, then 1.5 gm daily for 5 days and 1 gm for 8 days)

Towards the end of October, he had another attack, again treated with quinine (1.5 gm daily for 4 days), followed by mepacrine (0.1 gm three times daily for 5 days). A third attack occurred in December (similarly treated), and a fourth in January the latter was mild and responded well to quinine. The author had a mild febrile attack in February, and in March yet another appeared. He then procured some Paludrine and took the recommended dosage of 3 tablets of 0.1 gm daily for 10 days. He took 15 days' holiday in the country and felt better than he had during the first six months of his leave.

In the middle of May, 6 weeks after the course of Paludrine, he developed another attack having no Paludrine at hand, he used quinine again. On this occasion blood films showed many amoeboid forms of *P. vivax* showing the "tenacity of the infection and the failure of the 'suppressive course' of Paludrine."

After this attack was treated with quinine [dosage not stated] together with Stovarsol the author took Paludrine again in a dose of 1 tablet twice weekly or 6 months. He notes that his wife had attacks comparable to his own, with elapses throughout their leave. She however, took the first "suppressive course of Paludrine in the form of 30 tablets in 15 days instead of in 10 her lapse occurred five days after that of her husband.

The author points to the importance of recognizing relapsing *P. vivax* infection in persons returned from the Tropics and of the need for a prolonged course of Paludrine

H J O'D Burke-Gaffney

KONINKLIJKE VEREENIGING INDISCH INSTITUUT (voorheen Koloniaal Instituut) Amsterdam Mededeeling No 70 Afdeling Instituut voor Tropische Hygiene No 17 De behandeling van malaria met kinine met de techniek van het bloedonderzoek door Dr C W F WINCKEL [Treatment of Malaria with Quinine Blood Examination.] 46 pp, 6 figs & 6 coloured pls [Refs in footnotes] 1947, Amsterdam Indisch Instituut

Doctors have to be on the alert to recognize and to treat malaria because so many persons returning from Netherlands India and from confinement during Japanese occupation are arriving in Holland. This brochure is simply and clearly set out for the use of those who are not familiar with the subject in the

home country. Quinine treatment is stressed particularly for quinine is regarded as an essentially national medicine. The short cure is advocated and, as example, this may be given for benign tertian malaria — 1 dose of quinine hydrochloride or quinine sulphate of one gramme daily is administered until the temperature is normal and then one gramme daily is given in continuation for 5 days. This usually means a total treatment of 6 to 8 days. If a relapse occurs, precisely the same treatment is carried out and so with each relapse. No advantage is claimed for quinine hydrochloride or bisulphate which are more soluble, over the less soluble quinine sulphate. Diagrams are given to explain the method of intramuscular administration and a series of six coloured plates at the end show for *P. vivax*, *malariae*, *falciparum* and *ovale* the stages from young rings through amoeboid forms with Schüffner's stippling, schizont and morula, to male and female gametocytes. Three of the plates are those of thick drop appearances and a final table sets out differentially the appearance of each species of malaria parasite in stained films.

W. F. Harvey

STRAMAN, J. H. Quinine by Continuous Intravenous Drip in the Treatment of Acute Falciparum Malaria. *Trans. Roy. Soc. Trop. Med. & Hyg.* 1948, Mar. v. 41, No. 5 669-76. [20 refs.]

During the Japanese occupation of Malaya, the author was able to observe the records of nearly 2,000 cases of acute *Plasmodium falciparum* malaria in malnourished British, Australian and Dutch prisoners near Singapore. Treatment was based on quinine followed so long as stocks lasted, by mepracrine and plasmoquine. Severe infections were treated with quinine by intramuscular or intravenous injection—the latter almost entirely by standard methods. This paper records clinical and parasitological details of 15 patients treated by a continuous intravenous drip technique.

Approximately 1,000 cases were seen between February 1942 and September 1944—the majority were in 1942, one of the worst periods of malnutrition. No record of the number of intravenous injections is available but it is small. Solution for injection contained 1 grain of the bishydrochloride in 2 cc. of saline the rate of injection being 2 cc. a minute and the usual single dose 0.5 to 0.68 gramme. Four fatalities which were apparently due to this method are recorded, namely—

1. Heavy infection with *P. falciparum*. Intravenous injection 0.5 gm. immediate epileptiform convulsions and death.
2. Very heavy infection with *P. falciparum*. Intramuscular quinine 0.3 gm., followed in 1 hour by 0.2 gm. intravenously, 20 minutes later collapse and death.
3. Moderate *P. falciparum* infection. died during an intravenous injection (dose not given).
4. Heavy *P. falciparum* infection. 1.0 gm. quinine intravenously in 5 c.c. water. Immediate epileptiform convulsions and death. a large and concentrated dose.

In addition, there was a case of *P. falciparum* malaria in which during mepracrine treatment a convulsion occurred and death followed immediately after 0.3 gm. quinine intravenously.

Approximately 1,000 other cases were admitted between October 1944 and September 1945. Usually all these with over 100 parasites per thick field (Fick's method) were given 14 lumbar intramuscular injections of 0.5 gm. quinine. When the thick film showed considerably more than this number a parasite count was made. When this was over 100,000 parasites per cmm. (estimated by total red cell counts and the number of trophozoites per 100 red

cells) intravenous drip quinine was given regardless of the clinical condition, and also where cerebral or other pernicious signs were present. A Soluvac or Vacolite gravity flask, with drip regulator and tied-in cannula was used. The vehicle was sterile normal saline, sometimes with an intravenous preparation of thiamin added. In each case, 2 gm of quinine bihydrochloride were given in 24 hours, 0.5 to 0.66 gm per litre. The rate of flow was 30 to 40 drops per minute. The long saphenous vein at the ankle was chosen for injection, to allow use of the arms. The leg was placed on a back splint with a footpiece. The drip was continued for 12 to 96 hours, according to the severity of the case. 15 cases so treated are described in detail. The advantages of this method were (a) ease of combination with other treatment, thus 2 patients received 600 cc of blood for gross anaemia, (b) certainty of complete absorption, (c) certainty of a constant safe concentration of quinine without degeneration products producing inefficiency, (d) absence of unpleasant after-effects.

The disadvantage was some mild phlebitis of the vein when the cannula was *in situ* for 2 or 3 days, with risk of severe septic phlebitis. Of the 15 patients so treated two died, one on the 3rd day from tonic spasm, 3 hours after starting the drip, the second from pyaemia due to sepsis at the site of the drip on the 28th day. This patient on admission had 1,240,000 parasites per cmm of blood, while four had over 500,000, and all were in very poor condition.

FIELD and NIVEN [this *Bulletin*, 1937, v 34, 615] in an analysis of 750 cases of *P. falciparum* malaria on the 1st day of treatment concluded that 750,000 parasites per cmm in the peripheral blood was about the extreme limit of tolerance in Asian adults for the Malayan strain, and FIELD in a series of 2,000 cases records no recoveries where the count exceeded this figure (unpublished). A combination of starvation with a heavy malarial infection is very dangerous. FERNANDO and SANDARASAGARA in Colombo [*ibid.*, 1936, v 33, 687] found that intravenous quinine was contraindicated when the systolic blood pressure was below 90. The author considers that the drip method of using intravenous quinine in a dilute form sufficient to secure administration of 2 gm in 24 hours is a safe and efficient one. Recovery is recorded of 3 cases with a peripheral intensity of infection higher than has been hitherto recorded in Malaya (871,000, 925,000, and 662,000 parasites per cmm respectively).

JAILER J W, ROSENFELD M & SHANNON, J A. The Influence of Orally Administered Alkali and Acid on the Renal Excretion of Quinacrine, Chloroquine and Santoquine. *J Clin Investigation* 1947, Nov, v 26, No 6, 1168-72 [11 refs]. C F Shelton

HAAG *et al* (*J Pharm & Exper Therap*, 1943 v 79, 136) found that the urinary excretion of quinine given orally in a single dose was related to the pH of the urine the output being increased if it were made acid. Other authors [this *Bulletin* 1945 v 42, 780] have drawn attention to the correlation between urinary output of quinacrine (atebrin mepacrine) and ammonia. The effect of alkali and acid given by mouth on the urinary excretion of quinacrine, chloroquine and santoquine (the two latter being antimalarials of the 4-aminoquinoline series) has now been investigated. The patients were in the older age groups and the drugs were given orally in high initial dose on the first day, followed by a smaller maintenance dose on several succeeding days till the plasma levels were fairly constant. Sodium bicarbonate was given during the day in seven doses of 2.5 gm and a similar dose during the night (total 20 gm), which raised the pH of urine to 7.5 or 8. Ammonium chloride, as the acid, was given.

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W. F. Harvey

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- 1 Heavy infection with *P. falciparum*. Intravenous injection 0.5 gm. immediate epileptiform convulsions and death.
- 2 Very heavy infection with *P. falciparum*. Intramuscular quinine 0.66 gm., followed in 1 hour by 0.2 gm. intravenously. 20 minutes later collapse and death.
- 3 Moderate *P. falciparum* infection. Died during an intravenous injection (dose not given).
- 4 Heavy *P. falciparum* infection. 1.0 gm. quinine intravenously in 5 cc. water. Immediate epileptiform convulsions and death (a large and concentrated dose).

In addition, there was a case of *P. falciparum* malaria in which during mepracrine treatment a convulsion occurred and death followed immediately after 0.5 gm. quinine intravenously.

Approximately 1,000 other cases were admitted between October 1944 and September 1945. Usually all these with over 100 parasites per thick field (Field's method) were given a preliminary intramuscular injection of 0.5 gm. quinine. When the thick film showed considerably more than this number a paracetamol was made. Where this was over 300,000 parasites per mm. (estimated by total red cell counts and the number of trophozoites per 100 red

They then report the results of a number of experiments with paludrine. A patient was infected with the Rumaman strain of *P falciparum*. The primary attack and the first two relapses [= recrudescences] were lightly treated with paludrine or quinine. The third relapse was allowed to proceed unchecked and it produced a good crop of gametocytes, which readily infected a control batch of mosquitoes—*Anopheles maculipennis* var *atroparvus* (87.5 per cent positive). Paludrine was then given in two divided doses of 0.4 gm each and batches of mosquitoes were fed daily on the patient for 8 days after the administration of the drug and again on the 12th day. Samples of mosquitoes were dissected at appropriate intervals and the results indicated that up to and including the seventh day after paludrine, the mosquitoes failed to become infective—thus confirming Farley's work at Cairns [this *Bulletin*, 1946, v 43, 527].

Exflagellation of the male crescent occurred normally, and ookinets were plentiful in all the experiments, and the first indication that paludrine was having an adverse effect, was the small number of oocysts appearing on the wall of the mid gut. The authors suggest that it is the females upon which the drug acts, without however giving any very satisfactory proof.

[The planning of this experiment is perhaps not quite satisfactory, as the control only refers to the conditions prevailing at the very beginning of the "crescent wave". It is important to view all work relating to the sexual phase of *P falciparum* against the highly characteristic background of this phenomenon—as described for instance by the reviewer (this *Bulletin*, 1931, v 28, 995).] P C C Garnham

FARRELL, E. The *Anopheles gambiae* Problem in Brazil and West Africa, 1941-44. *Bull U S Army Med Dept* 1948, Feb, v 8, No 2, 110-24, 11 figs [Refs in footnotes]

Following the "unparalleled disaster" for the inhabitants of certain of the north-eastern states of Brazil because of *gambiae*-transmitted malaria, the joint efforts of the Rockefeller Foundation and the Brazilian Government had by 1940 eradicated *A. gambiae* from Brazil, "one of the finest public health achievements of the age". During the recent war, Brazil lay astride the heavily used airborne traffic routes from the U.S.A. and the Caribbean to the Mediterranean and Middle East Theatres of War via Senegal or Liberia or the Gold Coast.

The introduction of *A. gambiae* by air traffic to Brazil and the Caribbean was therefore an ever-present possibility. Indeed, with increase in this traffic, the Brazilian Port Health Service became increasingly alarmed at the numbers of *A. gambiae* found in aircraft arriving from Africa. Despite heavy penalties, the ordinance—which required incoming pilots to keep canopies down and cabin windows closed until the plane had been sprayed by Brazilian staff—was not completely effective, the escape of a single gravid female *A. gambiae* to areas beyond the controlled precincts of the airport might well mean disaster for Brazil.

Numbers of *A. gambiae* reaching Brazil became so alarming that the Brazilian Government, through both military and diplomatic channels, made representations to the Secretary of State, U.S.A. As a result, the U.S. War Department took special action and sent a small expert Commission to investigate the situation. This Commission reported in December 1943, that 'the cause of Brazil's *gambiae* problem lay not so much in neglect of current aircraft spraying regulations as in the neglect of environmental sanitation at West African airfields of departure, where *gambiae* mosquitoes were breeding in large numbers in the immediate vicinity of aircraft parked overnight prior to take-off for

The later history of the 20 patients is shown in a figure, which reveals that 19 of the infectious "held their own with scarcely a ripple in the relapse rhythm" which continued unchecked.

Referring to the very large numbers of cases of relapsing *P. vivax* malaria which will be seen in Britain and America for the next few years, and which will be given varied forms of treatment, the authors "trust that the fortune of those who pin their faith on neo-arsphenamine will be better than ours"

H. J. O'D. Burke-Gaffney

JANG C. S., FU F. Y. HUANG K. C. & WANG, C. Y. Pharmacology of Ch ang Shan (*Dickroa fersifuga*) a Chinese Antimalarial Herb. [Correspondence.] *Nature* 1948, Mar 13, 400-401

A number of papers have recently appeared (this *Bulletin*, 1948, v 43 1012 1947 v 44 669 964) dealing with the antimalarial action and chemical nature of the substances present in the herb (*Dickroa fersifuga*) which has been used in the treatment of malarial fevers in China for centuries. Extracts of the roots (Ch ang Shan) and more especially of the leaves (Shan Chi) have been found by the present authors to be active in *P. gallinaceum* infections of chickens. In all, 5 alkaloids, dichroline  $\alpha$ ,  $\beta$  and  $\gamma$  (which are quinasoline derivatives) dichroline and quinasoline and two neutral substances, dichroin A (4-hydroxy coumarin) and dichroin B have been obtained from the roots. The first three alkaloids are isomers and are mutually convertible under appropriate conditions. With the probable exception of dichroline  $\alpha$  all the isolated substances are stated to possess activity against *P. gallinaceum*. Some chemical and pharmacological properties of the seven substances are given in a table which, however is not very informative. Marked activity in *P. gallinaceum* infections has also been observed in an alkaloidal fraction from another Chinese herb Tou Ch ang Shan (*Hydrangea umbellata*?) which is related to *Dickroa fersifuga* and from it the authors have succeeded in isolating several alkaloids.

In an added note Dr T. S. Work briefly comments on the chemical aspects of the problem.

J. D. Fulton

HENRY A. F. V. Pré-ménothérapie catalytique des paludisme subaigu et d paludisme chronique (Hémochromatophtéropathologie) [Catalytic Pre-munition in Subacute and Acute Malaria (Hemochromatophtéropathology)] *Cahiers Méd. Union Française*, Algiers, 1947 Dec., 2, 2, 15 719-25

SHUTE P. G. & MARTON M. The Gametocytocidal Action of Paludrine upon Infections of *Plasmodium falciparum*. *Parasitology* 1948, F b 38, No. 4 284-9

The authors summarize the action of the old anti-malarial drugs on the gametocytes (crescents) of *Plasmodium falciparum* as follows —

<i>Quinine</i> Heavy doses 30 grains daily Very small dose	During 1st and 2nd days Later in attack Throughout	Crescent much reduced Crescents unaffected Crescent numerous
<i>Synpharmacin</i> 10 grs.	During 1st day of fever	Crescent is very numerous
<i>M. falciparum</i> Very small dose Larger doses 0.4-0.8 grs.	During 2nd and 3rd days do do 6th or 10th day	Crescent numerous Crescents less numerous Crescents numerous
<i>Plasmoquine</i> Very small doses	Any time	Crescents sterile



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would be necessary with simple oil larvicides. As against this, the method requires better trained control men, is dependent on the type of breeze, and the treatment has little effect on pupae.

Details are also given of the equipment and method of application of the DDT-oil spray technique from aeroplanes.

H S Larson

HIGMAN E. H. Recent Trends in Malaria Control in Latin America. *Mosquito News* 1947 Dec., v 7 No. 4 144-51. [12 refs.]

PARAENSE W. L. Estudos sobre o ciclo exoeritrocitário do *Plasmodium gallinaceum*. [Exoerythrocytic Cycle of *P. gallinaceum*.] *Mém. Inst. Oswaldo Cruz* 1947 Mar., v 45 No. 1 101-18. [13 refs.]

A general discussion on the development of exoerythrocytic forms of *P. gallinaceum* following blood and sporozoite inoculations, and the influence of quinine in suppressing the blood infection and permitting the development of fatal exoerythrocytic infection [this *Bulletin* 1948, v 45, p. 47]

C M Wenyon

LEWERT R. M. Alterations in the Development of *Plasmodium gallinaceum* following Passage through Tissue Culture. *Science* 1948, Mar 5 250

*Plasmodium gallinaceum* was grown in tissue culture according to the technique of GREY and GREY (*Amer J Cancer* 1936, v 27 1) the culture being started either from infected pia mater or from heart muscle. Extensive development did not occur but growth of the parasite continued for as long as 70 days after several subcultures. However the interesting part of this work lies in the results of the inoculation of these cultures into chicks 7-32 days old. The chicks invariably developed an infection of an exclusively exoerythrocytic nature and overwhelming in intensity. No pigmented parasites were ever seen, though in several instances a low percentage of the erythrocytes contained minute multinuclear forms. This peculiar type of infection was maintained unchanged through 9 passages, when intraperitoneal subinoculations of brain emulsions were employed. When blood instead of brain was subinoculated from the same series of chicks, pigmented erythrocytic parasites reappeared by the third passage though even as late as the eighth, the infection continued to be preponderantly exoerythrocytic. It may be noted that by the employment of this technique parasites as young as four days can readily be found in the capillary endothelium of the brain.

P C C Garahan

# ERRATUM

In the abstract of the papers by SHORT *et al* this *Bulletin* 1948, 45 783 the reference to HUFF & COLSTON in line 4 should read (*J Parasitol* 1947 v 33, No. 8 Sect. 2 (Supp.) 77). An abstract of this paper will appear in the September number of this *Bulletin*.

## BLACKWATER FEVER

LINGS, P. A. propos d'un cas de fièvre bilieuse hémoglobinoïdique chez un enfant indigène. 'A Case of Blackwater Fever in an African Infant'. *Tr. S. B. de Med Trop*, 1917 Sept 30 & 27, No 1 285 S

The author describes a case of blackwater fever which occurred during an acute attack of *P. falciparum* malaria in an African child of 23 months in the Belgian Congo. The haemoglobinuria appeared a few hours after an injection of 0.5 gm of quinine. The patient fell ill several days after an attack of malaria and was given quinine 3 g by mouth daily, but without effect. It frequent but not universal, his father sought medical advice to the contrary.

After the attack of blackwater fever had been cured by local measures and the existing *P. falciparum* infection had been treated with meprazine the patient five days later developed another acute attack of malaria with *P. falciparum* in his blood. He suffered four more such attacks within the following year. Because of the exceptional danger of blackwater fever in a susceptible subject it was decided to try the effect of meprazine prophylaxis. The last attack was treated like it preceded with 0.1 gm of meprazine daily for 5 days followed by 0.01 gm of plasmoprine daily for 5 days, after which 0.1 gm of meprazine was given in the direct medical or nursing supervision every Monday and Thursday. No more malarial attacks have occurred, the blood has remained negative on five examination, and the spleen is not palpable. The child attends the dispensary regularly twice a week for meprazine prophylaxis and is in excellent health at the present age of 3 years and nine months. The author returns the danger of irregular quinine prophylaxis in Africans and the indiscriminate use of the drug without medical control.

The rarity of blackwater fever in Africans owing, to the 'premunition' established is well recognized. It is suggested that this exceptional case occurred because the patient's circumstances regarding frequent malarial attacks and the irregular taking of quinine were the same as those commonly encountered among Europeans who develop blackwater fever. *H. J. O'D. Barle Gaffney*

## LEWIS, H. Haemolytic System in the Blood of Malaria-Infected Monkeys

Correspondence. *Nature*, 1918 Apr 10 500

This is a preliminary report details of which will appear elsewhere of a haemolytic substance found in the blood, parasitized (*Plasmodium knowlesi*) monkey blood. The parasite seems to produce it or cause its appearance in the erythrocytes, which it destroys when its concentration is high. It is then released into the plasma. It does not appear to differ (except in its higher quantity) from a haemolytic substance obtained from normal blood and other tissues and previously reported by the author and Lewis (*Nature*, 1915, Oct. 27, 507). It has so far been characterized as an unsaturated monocarboxylic fatty acid having one double bond and the possible chain length C18. Its haemolytic activity is inhibited specifically by intestinal drugs.

The mechanism may be thought of as enabling the metabolic utilization of the red cell by the parasite. Malaria pigment which is a haematin compound, accentuates this mode of erythrocytic destruction by the parasite. Haematin has itself been found to be haemolytic *in vitro* in low concentrations and in sub-haemolytic concentrations it strongly potentiates the effect of the haemolytic substance now described.

The author notes that it might be interesting to study the quantitative relations of these two factors in the blood of persons suffering from blackwater fever.

*H. J. O'D. Barle Gaffney*

# TRYPANOSOMIASIS

LOURENÇO MARQUES. Conferência Intercolonial sobre Tripanosomíase, Lourenço Marques, 28 a 31 de Agosto de 1946. [Inter-Colonial Conference on Trypanosomiasis, Lourenço-Marques, 1946.] Vol. I 387 pp. Vol. II 458 pp. Numerous figs., maps & charts. 1947 Lourenço Marques Imprensa Nacional do Moçambique.

It is evident that the Conference which took place in Portuguese East Africa on trypanosomiasis in 1946 was important. It was attended by delegates from almost all parts of British and Portuguese Africa, in which tsetse occurs and among them there were men interested in human and animal medicine, entomology agriculture and administration.

The report of the Conference is in English and Portuguese, and every word, including small parts of the discussion, is set down in both languages. The report has, therefore, a tendency to be diffuse and it is not easy to extract the conclusions or to find which parts of it are of permanent value. Certain topics which were discussed more than once appear in several different places the table of contents is so brief that it does not give one much help.

Where Portuguese originals have been translated into English the language is generally good and clear. A few technical errors have been noted, for instance "ape" for "baboon" "locke" for "locks" and "oxen plague" for "rinder pest". The phrase "typical podagral lesions were found in cudos" is presumed to mean that foot lesions, characteristic of foot and mouth disease, were found in kudus.

The report is illustrated with numerous maps, many of them in colours and with half tone blocks of the delegates sitting at the conference. The general presentation of the report reflects great credit on the Government printer at Lourenço Marques.

The volumes contain valuable information on several sides of the subject which had previously been obscure. The coloured maps give the distribution of Gloss as a whole and of some of the species, also distribution of trypanosomiasis of man and animals. Some of them deal with parts of the world such as Angola, Swaziland and Portuguese East Africa, about which it has been difficult to get up-to-date information. We note also a report by HUNTER on the present distribution of *G. morsitans* along the Save River and on the possible danger of its extension to the lower part of the valley of the Limpopo.

There are two valuable contributions from CHOLIST of Southern Rhodesia. In the first he deals with the history of the distribution of *G. morsitans* and nagana in that territory much of his facts being gathered from the records of hunters and travellers about seventy to ninety years ago. It is evident that fly was driven back, probably because hunters and the great epidemic "rinder pest" in 1896 killed the game. The fly then commenced to re-occupy much territory. The second paper gives a general account of the measures, principally game exclusion and game destruction, which were undertaken to drive *G. morsitans* back again. This is a very important piece of work for Southern Rhodesia has recovered a much larger area from fly than has any other African territory. The present paper is the only general account of what has been done, and we feel that the matter deserves more than the three pages given to it. We understand that the cost of the operation was remarkably low but so that no information is given.

South African authors gave the conference an account of the use of DDT in mineral oil sprayed from the air against *G. phlebotomus* in a small game area in Zululand. The paper by DE TOIT gives most useful information on the practical measures undertaken, e.g. organization, spray formula, dosage, cost and the effect on the tsetse as measured by traps.

It is evident that the clinicians had a varied and stimulating day. SOUSA first discussed what criteria should be used in estimating a cure of Gambian sleeping sickness. RAMOS and ASSOREIRA passed on to consider blindness in this infection. It is attributable to 'trypanosomic opto-chiasmatic arachnoiditis'. This condition is apparently to be treated by intracarotid injections of trypanasamide, pen-carotid or even frontal craniotomy to eliminate adhesions in the opto-chiasmatic region. Penicillin when administered by the intravenous or intramuscular route is without effect on trypanosomiasis. If it is given intrathecally, the trypanosomes disappear temporarily from the cerebrospinal fluid but the course of the disease is not affected.

The report contains much else that is valuable, e.g. a discussion on the relation of tsetse problems to game and to reforestation, and a terse account by PORTS of the relation between fly and vegetation.

The formal recommendations of the conference appear to have been written in a conservative and somewhat platitudinous mood. Among the more interesting ones, there is a proposal for the rapid exchange of information between territories, both on the distribution of tsetse and trypanosomiasis and on the progress of measures of control. A list of Government organizations which should be kept informed has been drawn up, and the Government of the Colony of Mozambique is invited to approach the French and Belgian authorities asking them to participate in the exchange of information. It is also desirable that bibliographies and summaries of work published should be circulated. It does not appear to have been pointed out at the conference that some of these functions have been carried out not unsuccessfully by the *Tropical Diseases Bulletin* and its predecessor the *Sleeping Sickness Bulletin*, since the year 1908. There are also proposals for the use of uniform symbols in mapping the distribution of tsetse and trypanosomiasis. Such symbols are illustrated at the end of the Report. P. I. Burton

SANDGROUND, J. H. with the technical aid of ROSEY MAYNARD. Experimental Studies of an Old Strain of *Trypanosoma gambiense*. I. The Enhancement of its Virulence and the relationship of this Phenomenon to the Species of Polymorphic Trypanosomes of Africa. *Ann Trop Med & Parasit* 1947, Dec v 41, Nos 3/4 293-305, 2 figs on 1 pl. [27 refs]

While the trypanosomes of the *brucei* group are morphologically indistinguishable and therefore constitute only a single species on clinical and epidemiological grounds they are referable to distinct categories corresponding to *T. gambiense*, *T. rhodesiense* and *T. brucei*. The first two parasites differ not only in the degree of pathogenicity to man but also in their response to treatment with drugs and in virulence to laboratory rodents. In the last respect *T. rhodesiense* resembles *T. brucei* more closely than it resembles *T. gambiense*.

In the present paper, an account is given of the experimental transformation of a typical *T. gambiense* into a strain highly pathogenic for laboratory rodents. The original 'Nzale' strain was brought to the United States from the Belgian Congo where it was isolated from a wild *Glossina palpalis* into a guinea pig, and passed through other guinea pigs, as well as through man. Using a standard infection, produced by intraperitoneal inoculation of blood containing one million trypanosomes the author studied the behaviour of "Nzale" strain in laboratory rodents. The infection in guinea pigs was symptomless with an average duration of 78 days. In rabbits, mice and hamsters its course was even more benign usually terminating in spontaneous recovery, with trypanosomes rarely appearing in the blood. Adolescent rats (35-50 days

old) rarely showed signs of infection while trypanosomes were present in the blood in varying numbers, the average survival time of these animals being 163 days.

Since such benign infections in rodents were unsuitable for chemotherapeutic tests, it was decided to increase the virulence of this strain. Whereas rapid syringe-passages through rodents splenectomy and blockade of the reticulo-endothelial system, failed to produce the desired effect success was obtained by inoculation of nursing rats 17 days old, with a heavy suspension of trypanosomes from an adult rat. Some of the young rats were heavily infected after 3 days, their average survival time being 32 days. Further passages through young rats brought about a gradual increase in the virulence until the 7th serial passage, when the duration of the infection was reduced to three days. Infection of older rats with the modified strain described as "V" resulted in their death after 4 days while the original "Nzale" strain retained its non-pathogenic character throughout the experiments. The behaviour of "Nzale" and "V" strains in rodents was compared in parallel experiments. In mice infected with "V" strain, there was progressive parasitaemia terminating in the death of the animals by the 5th day while those infected with "Nzale" strain showed scanty trypanosomes or none at all and the majority of the animals survived. All rats infected with "V" strain died within 7 days, while those infected with "Nzale" had scanty infections and died at irregular periods between the 25th and 95th days of infection. The average survival time of hamsters infected with "V" strain was 18.8 days, these animals also showed evidence of involvement of the central nervous system. On the other hand, the "Nzale" strain produced no visible signs of infection in hamsters. In contrast to the avirulent effect of "Nzale" strain, "V" strain killed rabbits within 60 days, with symptoms of acute disease manifested by lymphadenopathy and atrophy of cardiac muscles. In guinea pigs the contrast between the two strains is less marked.

In addition to enhanced virulence, the "V" strain of *T. g. marseus* revealed changes in susceptibility to drugs and in general behaviour which were indistinguishable from those of a strain of *T. brucei* studied in the same laboratory. Like *T. brucei* it is sensitive to antypol (Bayer 205) and to stilbamidine but is not affected by the highest tolerated doses of tryparsamide.

The stability of strain "V" was demonstrated by failure to produce an attenuation after inoculation of small doses of trypanosomes into adult rat and after passages through various other rodents. On the other hand the experiment of enhancing the virulence of "Nzale" strain by inoculation of young rats was successfully repeated several times.

In conclusion, the author discusses the bearing of his experiment on the question regarding the phylogenetic relations of trypanosomes of the *brucei* group. Since in these experiments by controlled and reproducible laboratory procedures, a typically *gambiense* trypanosome has been modified to produce a strain characteristic in every way of *T. brucei* or of *T. hodesiensis* it is held that similar changes might occur under natural conditions. Furthermore the present findings seem to indicate that the age of the host might be a potent element in favouring the enhancement of virulence among trypanosomes. Consequently infection of young hosts may represent the means whereby virulent strains of the human trypanosomes of West Africa are produced in nature.

The author regards *T. g. marseus* and *T. hodesiensis* as mutant strains of a single species which the international zoological law of nomenclature would by reason of priority recognize as *T. brucei*. This view was freely expressed by the reviewer (see this Bulletin 1944 41:150).

C. I. Hume

BESSEMANS, A, WITTEBOLLE, P & BAERT, H, Mlle Etude, par la micro-manipulation, de la virulence d'un ou de plusieurs trypanosomes et de granules de sang trypanosé [A Study by Micromanipulation of the Virulence of Single or Several Trypanosomes and of Granules in the Associated Blood] *Rev Belge Sci Méd* 1946, Oct, v 17, No 5, 284-9 [29 refs]

A review is given of previous attempts to infect animals by few or single trypanosomes. Infections produced by single trypanosomes have been reported by various workers during the past thirty years. The present work was carried out with an arsenic-resistant strain of *T. gambiense*, with a normal strain of *T. gambiense* and with a Belgian strain of *T. equiperdum*. By means of a micromanipulator, trypanosomes were isolated from citrated blood and injected subcutaneously into other animals. Eight guinea-pigs were inoculated with 1 to 20 trypanosomes from the arsenic-resistant strain of *T. gambiense*, no infections resulted. Similarly, nine other guinea-pigs were inoculated with one to fifty parasites from the ordinary strain of *T. gambiense*, none became infected. With the strain of *T. equiperdum*, transmission to mice was achieved in one of 36 animals inoculated with a single trypanosome. With 2-5 trypanosomes, about 8 per cent of a limited number of animals became infected. But even with as many as 50 to 200 trypanosomes, failure to infect often occurred. Twenty mice were inoculated with the granules which occur in the blood of animals with trypanosomiasis. None of these animals became infected. In other experiments the blood taken from guinea-pigs during the lytic stages of the infection was not infective for mice although apparently it contained many trypanosomes. *F Hawking*

MORACZEWSKI, S A & KELSEY, F E Distribution and Rate of Metabolism of Phosphorus Compounds in *Trypanosoma equiperdum* *J Infect Dis* 1948, Jan-Feb, v 82, No 1, 45-51, 1 fig [15 refs]

A study has been made of the phosphorus metabolism of *T. equiperdum* *in vitro* and *in vivo*, with the aid of  $P^{32}$ , a radioactive isotope of the element. In the *in vitro* investigations trypanosomes were isolated by centrifugation from the blood of infected rats and were then suspended in a saline-phosphate medium containing 2 per cent protein at pH 7.6 to 7.8 and maintained at 37.5°C. The motility of the trypanosomes was impaired by repeated washing and their total phosphorus content was reduced.

In experiments with radioactive phosphorus the labelled element with an activity of 3 millicuries per mgm was added to the medium as phosphate, to give a concentration of 0.5 mgm phosphorus per cc. Total phosphorus was measured by chemical methods and radioactivity by means of a Geiger-Müller counter. A method based on that of SCHNEIDER (*J Biol Chem* 1945, v 161, 293) was used on aliquots of trypanosome suspensions to estimate the distribution of phosphorus in the acid-soluble, phospholipid, nucleic acid, and phosphoprotein fractions. In the *in vivo* experiments in which 10 mgm of labelled phosphorus, as neutral phosphate containing 20 millicuries of  $P^{32}$ , was given intraperitoneally to rats phosphorus was similarly estimated in the four different fractions of isolated trypanosomes in plasma and in homogenates of heart and liver. In view of the results of CHEN & GEILING (*Proc Soc Exper Biol & Med*, 1946, v 63, 486) who showed that a phosphorylating mechanism was concerned in the breakdown of glucose to pyruvic acid the authors believe that the acid-soluble fraction may contain the phosphorus compounds involved in this process. While the total P present in trypanosomes kept in presence of stable or radioactive phosphorus was similar, the distribution in the various

fractions was altered, as a result the authors believe of the greater concentration of phosphorus in the medium made necessary for the measurement of radioactivity. During *in vitro* experiments the trypanosomes became inactive and probably more permeable thus vitiating to some extent the measurement of phosphorus exchanges which the authors considered to be of negligible proportions. The exchanges in three of the fractions *in vivo* were very much greater than those *in vitro* when measured after injection of the infected animal with labelled phosphorus. The turnover was in fact greater in the case of the trypanosomes than in the host tissues and showed that the parasites could utilize the inorganic phosphorus present in plasma for the synthesis of organic compounds of this element.

J. D. Fallow

SPINKS, A. Persistence of Suramin Analogues in the Blood Stream. *Biochem. J.* 1948, v 4, No. 1, Proc. Biochem. Soc. 1.

GAGE, J. C., ROSE, F. L. & SCOTT, Mary M. The Estimation of Suramin (Astrypyl Bayer 205) in Plasma. *Biochem. J.* 1948, v 4, No. 1, Proc. Biochem. Soc.

CALDWELL, A. G. & WALLS, L. P. Potential Trypanocides of the N Heterocyclic Series. Part I. Phosphoribothioic Salts. *J. Chem. Soc.* 1948, 1154-9.

STYCKES, C. B., HADAWAY, A. B., BARLOW, F. & GALLEY, W. Field Experiments with DDT and Benzene Hexachloride against Tsetse (*Glossina palpalis*). *Bull. Entom. Res.* 1948, Feb., v 38, Pt 4 591-612, 4 maps, 3 text figs. & 3 figs. on 1 pl.

The five experiments described in this paper were performed in Uganda in 1946. Vegetation was sprayed with DDT and gammexane to a height of 6 feet. The first test took place on Nko, an unoccupied island of 100 acres in Lake Victoria, about a mile from the mainland, where the tsetse population was estimated to be 11,700. Gammexane (0.65 per cent gamma) in 50 per cent. kerosene and 50 per cent. cottonseed oil was applied by Four Oaks Ken sprayers at a rate of 2 1/2 quarts per 1,000 square feet. The selected patches amounted approximately to 2 acres. The fly reduction was estimated at 56 per cent. over a period of 10 days, after which the numbers began to increase. After 4 weeks they had reached pre-treatment numbers. The spraying was then repeated and some additional areas were included. For a week afterwards the reduction in fly density was about 60 per cent., but rose again. Deposits of gammexane on leaf surfaces of samples of treated vegetation were low even one day after application.

Areas of vegetation on another island, Mbirumbwa, about a mile from the mainland, were similarly treated this time with DDT (5 per cent in 50 per cent. kerosene and 50 per cent. cottonseed oil). About 17 acres of total of 30 acres were treated. Reduction of fly was estimated at 60 per cent. for a week, then the numbers increased. There seemed to be an appreciable loss of insecticide through penetration of the leaves.

In a later test on the same island, four applications of DDT were made at intervals of 10 to 14 days. The selected areas of vegetation along the coast and in the centre of the island amounted to about 4 acres. From the 6th to the 13th week after the final application, no flies were seen or caught, then flies were captured. Again there was considerable loss of insecticide from leaf surfaces some 1 ft through rain.

The last experiment was made at Nkuruba, a peninsula of the mainland, where a linear distance of about 9,000 yards was treated. Four applications of DDT were made the first two comprising 100 parts of DDT in 100 parts



used with an emulsifier) and two parts of lake water and the other two of 5 per cent DDT in deiselene. The movement of cattle and rainfall interfered with the trial to some extent, and as a result of the rainfall the growth of the vegetation was very rapid. The fly density was reduced by about 98 per cent but a week after the final application flies began to appear in fair numbers at some points. Insecticide deposits on sample papers and leaves were small, though the ATSO emulsion persisted for several weeks and gave fairly good kills. Deposits of 116 and 173 mgm per square foot on leaves of *Dracaena* gave kills of 100 per cent and 93 per cent respectively for 8 and 16 weeks afterwards. Deposits on hairy leaves gave negligible kills. The authors conclude that these rather laborious methods, even at excessive dosages, are not likely to eliminate *Glossina palpalis*. The experiments show that an insecticide is required that will not be absorbed by the vegetation, and that will not lose its toxicity, and a method will have to be devised that will give much greater coverage than can be achieved with small knapsack sprayers.

H S Leeson

LARANJA, F S, DIAS, E & NOBREGA, G. O eletrocardiograma na cardiopatia crônica da doença de Chagas [The Electrocardiogram in Chronic Cases of Chagas's Disease] *Brasil-Médico* 1948, Feb 21 & 28, v 62, Nos 8/9, 51-2 English version 52-3

This appears to be a summary of a paper presented to or read at an Inter-American Congress of Cardiology, held in Mexico in October 1946, and based on investigations carried out in Minas Gerais. The authors studied 357 cases of chronic Chagas's disease and electrocardiographic alterations were found in 208 (58.2 per cent) of them. These included extrasystole of ventricular origin, A-V blockage of different types, intraventricular block, nearly always of the right branch bundle (90 out of 92), QRS changes with or without T-wave alterations. P-wave alterations usually transient, and, less commonly, auricular fibrillation. Arrhythmia was present in just over half (52.9 per cent) of those with abnormal electrocardiogram, usually ventricular in origin, and the authors maintain that extrasystoles persisting after effort point strongly to cardiac involvement in patients with Chagas's disease. A-V block was observed in 21.5 per cent of those showing ECG abnormalities and this is regarded as an early change, so much so that when this symptom is found in patients under 40 years of age, other, confirmatory, signs of Chagas's disease should be looked for. Another peculiarity is the suddenness with which changes in the T-wave might be temporary and transient or permanent, like those seen in ischaemia of the anterior wall ("coronary T-wave"). Alterations of would show progression and retrogression in cycles which varied in different patients. In ordinary cases of Chagas's disease auricular fibrillation is not common but when present is of bad import, as Chagas himself noted, if, however it is associated with arteriosclerosis it may react to quinidine and, if prognosis is more favourable. Only slight changes are frequent in the P-wave, marked change is very rare [figures are not given].

H Harold Scott

## LEISHMANIASIS

SHI LU CHANG & NEGERBON W O Studies on Hemoflagellates. III. The Specificity of Serological Reactions of *Leishmania donovani* vs *L. brasiliensis*, *L. tropica* and *Trypanosoma cruzi*. *J Infect. Dis* 1947 Nov Dec. v 81 No. 3 209-27 10 figs. on 2 pls. [17 refs.]

Employing the culture method described in an earlier paper [this Bulletin, 1947 v 44 1055] the authors have tested the serological reactions of two strains of *Leishmania donovani* and *Trypanosoma cruzi* and of one strain of *L. brasiliensis* and *L. tropica*. Guinea-pigs were immunized against *T. cruzi* by injecting them intraperitoneally with living organisms or with 0.5 to 2 cc. of the packed killed organisms, it being estimated that 1 cc. contained 2,500,000,000 flagellates. The organisms were killed with formalin which was added to the washed suspension of flagellates to give a concentration of 0.025 per cent. or by heat, an exposure to 50-55°C. being given for 20 minutes. For the leishmania, only living organisms were used for immunization. Blood was taken from the guinea-pigs by heart puncture after the 6th, 8th and 13th injections of antigen given at intervals of three to four days. Agglutination tests were carried out with various dilutions of serum, the microslide test with living organisms giving the best results. In all cases, the sera gave a good agglutination with the homologous organism but a weaker agglutination was always given with the other organisms.

Furthermore, with increased dilution of the sera, the heterologous agglutination disappeared first, the homologous agglutination persisting at a + reaction with dilutions of 1 in 1,280 to 1 in 2,560. In the complement-fixation tests, both a glycerinated antigen and one prepared by lyophilizing thoroughly washed organisms suspended in normal saline were used. No significant difference in the potency of these antigens was noted. In the precipitation reaction the ring test was found to be the most delicate. The lytic effect of antisera at low dilutions could not be eliminated with the leishmania, but could be in the case of the more resistant *T. cruzi*. Absorption of antiserum with homologous antigen removed the species as well as the cross-reacting antibodies, while absorption of antiserum with heterologous antigen removed all of the respective antibody part of the cross-reacting antibodies and reduced the agglutination titre against the homologous antigen organisms. Ghost cells gave the same reactions as living cells, but a lower titre of the homologous antigen. The general result of the observations is that the culture forms of the organisms tested have both species-specific and common antigen and that the specific antigen is predominant while the common antigen is probably a combination of several antigen components. C M Heyson

## FEVERS OF THE TYPHUS GROUP

REVOL, L. COUDERT J & MOREL P Etude de la moelle osseuse par ponction sternale de neuf cas de typhus exanthématique. Study of the Bone Marrow obtained by Sternal Puncture in Nine Cases of Exanthematic Typhus. *Bull Soc Path Ex* 1947 v 40 Nos 11 12 479-82

The authors give a brief summary of the scanty literature dealing with the changes found in the bone marrow in typhus fever and then describe the conditions found in nine cases studied at the height of the attack.



JADIN J & GIROUD P. Typhus exanthématique de l'Urundi, agglutination des rickettsiales. (*Exanthématique Typhus in Urundi (Belgian Congo); Rickettsial Agglutination.*) *Bull. Soc. Path. Exot.* 1947 v 40 No. 11/12, 414-16.

An epidemic of typhus fever occurred in Urundi in 1945-1946, and 23 sera of patients from various localities were tested by the rickettsia-agglutination reaction. Eighteen of these sera agglutinated epidemic typhus rickettsiae at much higher titres than murine-typhus rickettsiae and only one gave a reaction suggestive of murine infection, the response being a titre of 1-8 400 with murine rickettsiae against one of 1-3,200 with epidemic rickettsiae.

John H D Meyer

RUIZ CASTANEDA, M. Preparation and Properties of Purified Rickettsial Suspensions. *J Immunology* 1948, Mar., v 58, No. 3, 283-92, 5 figs. [18 refs.]

Workers interested in the preparations of rickettsial antigen will wish to read this paper in the original text, in which the author gives details of his recent improvements in the methods of purifying and concentrating suspensions of epidemic and murine-typhus rickettsiae obtained from the lungs of mice and rats infected by the intranasal route.

The suspensions are used for agglutination, complement fixation opsonic, and allergic skin tests as well as for the preparation of vaccines.

The author remains convinced that his bivalent lung vaccine is preferable to the commonly used monovalent vaccines because murine rickettsiae can easily be obtained in large quantities from rat lungs, whereas epidemic rickettsiae have to be prepared from mouse lungs, and also because in Mexico, and perhaps in other countries, murine typhus is not only endemic but also epidemic when transmitted from man to man by lice.

The bivalent vaccine when given in three doses of 11 into each ear in Mexico but the author believes that a course of five doses given at weekly intervals will afford complete protection.

Photomicrographs are reproduced to show the morphological appearance of the rickettsiae as seen in stained smears and it is stated that the murine rickettsiae occur as small rods of uniform size, whereas the epidemic are pleomorphic and of variable size but most of them are larger than the murine.

John H D Meyer

WALKER, R H. Fatal Anaphylaxis following Typhus Vaccine Injection. *Lancet* 1948, May 1st, v 256, No. 6633, 1011.

FOX, J P & PETERSON O L. The Antirickettsial Effect of Thionine Dyes. II. On the Mode of Action of the Thionine Dyes in combating Experimental Infections of Mice with *Rickettsia orientalis* and *Rickettsia mooseri*. *J Immunology* 1948, Mar v 58, No. 3, 299-321 [33 refs.]

In this paper the authors describe the results of studies in continuation of those already reviewed in this Bulletin 1947 v 44 813.

Toxidine blue and methylene blue in suitable doses were found effective in combating rickettsial infection in Swiss mice. The strains tested were a hard strain of *Rickettsia orientalis* and two strains of *R. mooseri*.

A distinct, but less pronounced, effect was caused by six other related dyes: azure C, azure A, brilliant cresyl blue, azure B, thionin blue, and xelenin methylene blue. A number of other related compounds were found to be ineffective.

The mechanism of the anti-rickettsial effect of the drugs has not been explained, but it is thought to be associated with the chemical structure and known properties of the compounds. Full details are given of a large number of experiments, these, and the discussion of the mechanism of the action of the drugs, will be of special interest to workers on chemotherapy. Unfortunately the authors cannot hold out any hopes that any of the drugs tested will be useful in the treatment of human rickettsial diseases.

SAYERS, M H P & HILL, I G W. The Occurrence and Identification of the Typhus Group of Fevers in South East Asia Command (Written in 1945) *J Roy Army Med Corps* 1948, Jan, v 90, No 1, 6-22, 1 chart & 1 map [18 refs] John W D Megaw

This paper, written in 1945, contains a useful summary of the occurrence, geographical distribution, epidemiology, special features, and laboratory findings relating to the cases of fevers of the typhus group observed in the hospitals of the South-East Asia Command during the years 1941 to 1944. Almost all the information contained in the paper has already been published in articles which have been reviewed in this *Bulletin*. About 5,500 cases were diagnosed during the period and it can safely be assumed that more than 90 per cent of these were mite-borne. The only outbreak that can with reasonable certainty be regarded as tick-borne was a small group of 33 cases at Ranchi, Bihar, India, in 1943. In the other outbreaks there were a few scattered cases in which a predominating agglutination response of the *Proteus* OX2 type or of the combined OX2 and OX19 types suggested that the infection may have been tick-borne. There were also a few cases in which a response of the OX19 type was regarded by the author as evidence of flea-borne infection. [This type of response is regarded by American observers as occurring frequently in the tick-borne Rocky Mountain spotted fever.] John W D Megaw

HORTON, R G, KAREL, L & CHADWICK, L E. Toxicity of  $\gamma$ -Benzene Hexachloride in Clothing. *Science* 1948, Mar 5, 246-7

Tests conducted by the U S Department of Agriculture at Orlando, Florida, have shown that herringbone twill impregnated with 2.0 grams of  $\gamma$  isomer of hexachlorocyclohexane (G.B.H.) per square foot of cloth is highly effective against mites and withstands repeated laundering better than other mite impregnates. But unusual symptoms appeared in 2 workers engaged in preparing batches of the compound for field tests, which suggested that G.B.H. may be absorbed through the skin. In order to investigate this possibility, 40 per cent acetone solutions of the pure  $\gamma$  isomer, or of a mixture of hexachlorocyclohexanes containing 83 per cent  $\gamma$  isomer, were applied to the backs and sides of a variety of animals clipped or depilated 24 hours previously, care being taken to prevent ingestion or inhalation of the compound during the initial 72-hour period of observation. Herringbone twill cloths impregnated by spraying with, or by machine-dipping in, an acetone solution of G.B.H. (83 per cent  $\gamma$  isomer) of such strength as to yield a concentration of 2 grams of  $\gamma$  isomer per square foot of cloth, were also applied as snugly fitting coats, the covered area of clipped skin per unit body weight corresponding approximately to that for a man in a suit. A number of rabbits and rats died within a few days, displaying symptoms typical of parenterally administered G.B.H. Guinea-pigs were much less sensitive than the other species. The total loss of G.B.H. from the impregnated suits amounted to 17 per cent after one

23 per cent. after two wearings and 33 per cent. after three launderings and so wearings. Bodily motion seemed to contribute to an increased rate of absorption, presumably because small crystals flaked from the fibres and worked into the skin. The authors think it probable that  $\gamma$  benzene hexachloride can be used safely as an impregnate only at concentrations so low as to eliminate any advantages as an insecticide it might possess over other compounds under test.

G. R. Cameron

HUEBNER, R. J., HOTTELE, G. A. & ROBINSON, Eleanor B. Action of Streptomycin in Experimental Infection with Q Fever. *Pub. Health Rep. Wash.* 1948, Mar 19 v 63, No. 12 357-62.

Streptomycin has already been shown to have a strongly inhibiting effect on the organisms of epidemic typhus, endemic typhus, Rocky Mountain spotted fever and rickettsialpox [see this *Bulletin* 1948, v 45 321]. The authors have now found that the drug has a similar action on *Rickettsia burneti*.

With doses proportional to those commonly employed in human therapy the drug was found highly effective in the treatment of guinea-pigs infected with large doses of virulent *R. burneti*. The treatment, however, was started much earlier than would be possible when dealing with the disease in man.

A similar inhibiting effect was observed when the drug was injected into yolk sacs just before these were inoculated with *R. burneti*.

In both sets of experiments the action of the drug was rickettsiastatic, not rickettsiacidal.

John W. D. Murray

## YELLOW FEVER

VEGHEX RODRIGUEZ, A. Control del *Aedes aegypti* en Chile. [Control of *Aedes aegypti* in Chile.] *Bol. Oficina Sanitaria Panamericana*, 1947 Oct., 28, No. 10 832-3. English summary.

Although *Aedes aegypti* exists along the coast of Chile from Arica to Coquimbo there have been no outbreaks of yellow fever in that country for 35 years. Arica is an important land sea and air port and international crossroads in the extreme north of the country, and although the port itself is free from *Aedes*, the Department of Arica, with vast frontiers, adjoins endemic areas in neighbouring countries. The Chilean Government adheres strictly to existing conventions and has signed one recently with the Government of Peru and Bolivia regarding a campaign against the yellow fever vector.

The foci of *Aedes* in Arica at some 5 kilometres from the airport also sea-going vessels anchor 1 kilometre from the port for health inspection. Despite this, additional measures were introduced in a campaign started in Arica in 1946. These included revision of the census of wells, anti-larval measures, the use of DDT in dwellings and on water deposits, inspection of traffic, aerosol bomb fumigation of aircraft, health education and biological campaign, consisting of placing *Gambusia affinis* in every water pool or reservoir.

An *Aedes* index of 40 per cent. in 1945 was reduced to zero in January 1946, and is still maintained there. An outbreak of yellow fever in the Santa Cruz Department of Bolivia caused these measures to be intensified. In 1946 166 aircraft were inspected and insecticides applied. Vaccination against yellow fever is not provided in Chile: there is no necropsy service as no confirmed foci of jungle yellow fever have appeared in the country up to now.

H. J. O'D. Burke-Gaffney

## DENGUE AND ALLIED FEVERS

ROSS, S G Dengue Fever at Fanning Island (Central Pacific) *Med J Australia* 1948, Jan 17, v 1, No 3, 63-6, 2 figs

Among 46 cases of dengue seen at Fanning Island in 1946 and 1947 there were 32 that were "afebrile" or "nearly afebrile". Nearly all of these modified attacks occurred in persons who had already suffered from the disease during their stay on the island or before their arrival. Similar attacks occurred in two volunteers who allowed themselves to be bitten by experimentally infected *Aedes aegypti* mosquitoes. One of the volunteers had a typical attack of dengue five years previously, the other had a severe attack six months earlier.

The modified attacks rarely lasted more than four days, the temperature was usually normal, a rash was seen in five of the patients on the face, wrists or ankles, frequent and painful micturition was a prominent symptom, the pains and blood changes were of the types commonly observed in typical cases of dengue.

From a study of the cases the author concludes that there is support for "the theory of tolerance to the virus of dengue after reinfections", but he thinks it probable that "a few different immunological strains of dengue virus are present at Fanning Island" because he saw a few cases of the modified type among persons who had had no previous attacks. *John W D Magaw*

MARIOTTI, M Febbre da pappataci e febbre delle macerie con eritema persistente facciale quale utile segno di diagnosi postuma [Sandfly Fever with Persistent Facial Erythema as a Useful Diagnostic Sign] *Acta Med Italica* 1948, Jan. v 3 Supp No 1 26-35 English summary (7 lines)

## PLAGUE

GIRARD, G Sur un point de terminologie l'expression *peste sylvatique* ou *sylvatique* est fondamentalement erronée ["Sylvatic Plague" an Error] *Bull Soc Path Exot* 1948, v 41, Nos 1/2, 15-16

A fundamental error in terminology which has gained 20 years start may simply have to be accepted. Girard, however, calls attention to the derivation of the word "sylvatic" from the Spanish *selva* and the Latin *silva*, a wood, and contends rightly that the rodent vectors of this form of plague inhabit steppes and not forests. Sylvatic plague rodents are the tarbagan, the spermophil, the squirrel, the gerbil, the multimammate mouse, and the cui—they dwell in the steppes of Asia or Russia, the plains of America, the deserts of Africa, and the veld of South Africa. Similar objections were taken to the word "Sylvatic" by Adolfo Pozzo [this *Bulletin*, 1946, v 43, 880] who suggested the description "rural" plague as the antithesis to "port" or "urban" plague. That may apply to South America, but would not apply universally. In fact, Girard maintains that all plague, at least in North Africa, in French West Africa, in Madagascar, in the Netherlands Indies or in British India, whether it be plague of town, village, or jungle hamlet, is murine, and that the only reservoir is the domestic rat. It suffices then to distinguish plague rodents simply as wild and domestic. *W F Harvey*

HERRIVAUX, A. & TOUMAROFF C. *Epidémiologie de la peste à Saigon-Cholon* (1943). L'étude de la faune pulicéenne des rats dans ses rapports avec la transmission de la peste. [Rat Fleas and Plague in Saigon.] *Bull. Soc. Path. Exot.* 1948, v 41 Nos. 1/2, 47-59 [12 refs.]

An epidemic of 42 cases of plague in 1943 with 5 sporadic cases in 1944 was the subject of study by the authors. Their tabulated results are presented for rats, mice and muskrats respectively. A hint of caution is thrown out as to deductions from these figures for the *X. cheopis* index of the epidemic was only 2.63 and never reached the annual mean figure of 5 per rat, which is said to represent an epidemic danger point. The authors found that on all the animals *X. cheopis* was the predominant flea: there was no correlation between the index and the course of the epidemic. *X. cheopis* was the predominant flea on the mice and *Leptopylla musculi* was never seen on this animal. *Cimex cephalus* fleas of dogs and cats seemed to have a seasonal prevalence opposite to that of *X. cheopis*. *X. astus* played a feeble, if any part as a plague vector.

W. F. Harvey

SHARIF M. Nutritional Requirements of Flea Larvae, and their bearing on the Specific Distribution and Host Preferences of the Three Indian Species of *Xenopsylla* (Siphonaptera). *Parasitology* 1948, Feb., v 38, No. 4 253-63. [41 refs.]

Much experimentation by the author has shown that a mixture of dried blood and yeast provides an ideal food for flea larvae and this has been used as control diet for comparison with other possible diets. The results obtained have been checked statistically for significance and relate in particular to the 3 species of *Xenopsylla* found in India: *cheopis brasiliensis* and *astus*. The irregular distribution, especially of *cheopis* and *astus* has been the subject of much discussion, as also has the question of the possibility of survival of fleas and their larvae in grain in course of shipment to distant places. In this research attention was concentrated on the suitability of various foods for the flea larvae as judged by the duration of larval life up to the beginning of pupation or cocoon formation. Ordinarily flea larvae feed on decaying organic matter containing microorganisms and it has been determined that their principal requirements are proteins and vitamins. The test and control diets used were (a) blood alone (b) highly milled wheat flour devoid of bran, (c) blood and wheat flour and (d) blood and yeast. One general fact emerged from these experiments, that the deep brown colour and sclerotization of adult fleas obtained from larvae of all three species depended on the presence of haemoglobin in the diets, which again, it is suggested, is dependent on the iron content of the haemoglobin.

The results of the tests were that pure blood was inadequate as a diet for flea larvae probably owing to deficiency in vitamin. Growth of larvae on pure wheat flour was erratic and probably necessitated the presence of microorganisms. Thus point, the presence of microorganisms, whether fungi or yeast is evidently one of great importance and was exemplified by the fact that a mixture of blood and wheat flour although quickening larval development was not a satisfactory diet. The conclusion is drawn that larval diets containing blood or wheat proteins and vitamins of the B group are essential for the successful rearing of these rat fleas. From the tests also certain conclusions could be reasonably drawn as to the distribution and host preferences of adult fleas thus: *X. astus* will flourish in the burrows of *Tatera indica* and *Bandicota mussharti*, because these provide the larvae with rich food. On the other hand, *X. cheopis* and *X. brasiliensis* larvae will subsist and develop on much simpler diet and prosper readily in a burrow of the domestic rat.



even where the nutritive value of the larval food is very low " Temperature tolerance is a factor which is lowest for *X brasiliensis* and this leaves *X cheopis* as the flea with a probably wider distribution because of the simpler larval requirements than either of the other two As *X brasiliensis* and *X cheopis* larvae grow better than *X astia* on flour alone, " this possibly enables them to survive transport in grain even without rats, to places far from their original home " W F Harvey

QUAN, S F, FOSTER, L E, LARSON, A & MEYER, K F **Streptomycin in Experimental Plague** *Proc Soc Exper Biol & Med* 1947, Dec, v 66, No 3, 528-32, 4 figs

Streptomycin, if available, may replace sulphadiazine in the treatment of plague, or possibly, be used along with a sulphonamide and with serum Details are given of (1) *Results obtained in vitro* These showed that streptomycin was bactericidal and appeared to be more active on virulent strains (2) *Effect on mice and guinea-pigs infected subcutaneously* The treatment was by subcutaneous injection, was post-infectious (48 hours), and was more effective than sulphonamide treatment (3) *Effect on septicaemic plague in mice* Cure was obtained in 80 to 90 per cent of non-bubonic septicaemic plague infections, of a type resembling the clinical form of human septicaemic plague, if the treatment was begun early and the doses large (4) *Effect on pneumonic plague in mice* " As might be expected 200 to 400 µg of streptomycin hydrochloride every 6 hours, effectively cure 90 to 95 per cent of the infections " Smaller doses and delay in treatment reduce the chance of cure (5) *Suggested schedule of treatment in human plague* Streptomycin, the most effective therapeutic agent yet discovered " for the treatment of bubonic, septicaemic and pneumonic experimental plague infections in mice and guinea-pigs ", should be given in human plague at the earliest diagnosis, in daily doses subcutaneously of 2 gm in bubonic plague, 4 to 6 gm in septicaemic and pneumonic plague The intervals of injection should be 4-6 hours for the first two days, after which the dose may be reduced It is recommended, however, that to prevent recurrence one gramme should be continued daily for at least 8 days, unless it is more convenient to substitute sulphonamide therapy at this stage The simultaneous administration of potent antiplague serum may be required in profound toxæmia W F Harvey

POLLOCK, J S M **Plague controlled in Haifa by the Use of DDT alone** *Trans Roy Soc Trop Med & Hyg* 1948, Mar, v 41, No 5, 647-56, 2 figs

The efficient control of human plague would seem to be in sight, and the author hopes that " the world has seen its last widespread plague epidemic " Immediate measures are designed to break the rat-flea-man chain by attacking the flea with DDT Treatment of patients proceeds as usual, reliance being placed on sulphadiazine and streptomycin Long term measures may be taken up, as and when possible Experience in previous outbreaks was of thousands of pounds spent on anti-plague measures and yet without influence on the course of the epidemic

Haifa is probably a fairly typical Turkish town of olden times A main paved sewer runs from end to end of the old city and from May till November never runs full Its sides are shelved and give both ideal runways and breeding places for the sewer rat Dwellings are crowded, each has a dark damp basement, which is, under present circumstances, itself a human habitation and has direct branch communication with the main sewer The

port of Haifa on the other hand is quite modern, but is closely linked with the old city. It is a busy inward and outward port and is provided with extensive grain and food stores.

The first case of bubonic plague in the outbreak under review was admitted on 26th June 1947 and proved fatal. Full-scale plague precautions were immediately taken in five sectors of the city, in each of which a DDT team laid down 5 per cent. residual spray using the Four Oaks knapsack sprayer. Impediments were cleared by labourers. A sixth team was mobile for the spraying of "house and work place of each suspected case and their surroundings. It was possible with this organization to lay down 500 gallons of DDT spray daily. At the same time, great publicity was given to the need for residual spray in houses, and 10 per cent. dusting powder for bodily use. Centres were set up at which power-driven compressor blowers were used for dusting purposes and these centres became very popular with the specially important lower class, Arab population. As many as 30 000 persons were dusted in the first 10 days.

The last plague case seems to have occurred on 19th July. "In all nineteen bacteriologically proved cases of plague were treated in the Government Hospital, Haifa" all of them were bubonic. Six other cases were clinically bubonic, but not proven bacteriologically. Only one case the first proved fatal. The circumstantial evidence produced in this outbreak would indicate that by using DDT as the first line of attack together with a modified cordon sanitaire rat extermination, while important, may take secondary place and should be planned on a long term continuous preventative basis."

W. F. Harvey

NICHOLSON H. P. & GAINES T. B. A Comparison of the Effectiveness of 5 and 10 per cent. DDT Dusts for the Control of Rat Fleas. *Pub Health Rep Wash.* 1948, Jan. 30 v. 63 No. 5 129-33, 4 figs.

Field studies were made in July 1946 at Columbia, S.C. U.S.A. to determine the value of dust containing 5 per cent. DDT and 95 per cent. pyrophyllite for the control of rat fleas, and to compare the results with those obtained in 1945 in Savannah, Ga. where 10 per cent. DDT dust was used.

The rat infested establishments were shops, cafés, warehouses, etc. in both places, and similar premises were used as checks. The insecticide was piped to the rat burrows by dust gun and to the runs by shaker. Photographs of this equipment are given. All rats trapped (except six *Rattus uticus* in the Savannah test) were *Rattus norvegicus*. The fleas were predominantly *Xenopsylla cheopis* the following species being rare both in treated and untreated establishments: *Xenopsylla fasciatus*, *Leptopsylla segnis*, *Echimopsylla gallinacea* and *Cimex cephalotes*.

The rats were trapped before treatment & 8 to 8 days after treatment, then at intervals of 6 weeks for about three months. Because of the scarcity of other species, comparison of results is based on the effects on *X. cheopis*.

The rat flea populations were almost completely eliminated within a week after application of both the 5 per cent. and the 10 per cent. DDT dusts in every type of treated premises. There was no significant degree of recovery after three months and no significant difference in the results of the two formulations. The maximum duration of effective control could not be determined.

H. S. Lorton

## CHOLERA

UNDERWOOD, E A *The History of Cholera in Great Britain* *Proc Roy Soc Med* 1948, Mar, v 41, No 3, 165-73 (Sect Epidem & State Med 1-9), 1 fig [37 refs]

The history of cholera in Great Britain is one of little more than 100 years. True cholera was known as Asiatic and on its arrival had to be distinguished from the simple indigenous "cholera nostras". The first death from true cholera in Britain occurred in Sunderland on October 20, 1831. Cholera then spread epidemically, affecting the north of England and south and mid-Scotland, later it spread to England generally. At first cholera was regarded as a visitation of Divine Providence and as a catastrophe in the lives of the poor. This opinion seems to have changed somewhat when cholera became a pestilence sparing "neither age nor sex nor station". Much discussion raged on whether cholera could be called contagious and Snow's essay of 1849 was entitled "On the Mode of Communication of Cholera", it was followed by his further publications. He asserted his belief that the excretions of the sick contained the contaminating material and by multiplication the doctrine of water-borne cholera, which received strong support from the episode of the Broad Street Pump in St James's Parish in London. The Board of Guardians ordered removal of the pump handle and the incidence of new cases in this area ceased almost at once. The epidemics of cholera in Great Britain caused "the deaths in England and Wales alone of 21,800 persons in 1832 53,292 in 1848-49 20,099 in 1853-54 and 14 378 in 1866". The 1832 epidemic and subsequent visitations have close connexions with the establishment of social reforms formation of the great Prudential Insurance Company and the building up of "quarantine and other measures which have kept this island almost inviolate for eighty years".

W F Harvey

TAYLOR, J *Epidemiology of Cholera* [Summary] *Proc Roy Soc Med* 1948, Mar, v 41, No 3, 174-6 (Sect Epidem & State Med 10-12)

Most of the points made in this important communication have already been summarized [see this *Bulletin* 1948 v 45, 175]. It may be well to add that the actual mode of introduction into Egypt of the first infection has not been established. "So far we have no definite information on how infection was introduced to Egypt at a time when the disease had not been reported as occurring in any other country west of India. Air or sea carriage from the East must be presumed".

W F Harvey

WHITE, P B *Bacteriological and Immunological Aspects of Cholera* [Summary] *Proc Roy Soc Med* 1948, Mar v 41, No 3, 176-7 (Sect Epidem & State Med 12-13)

A remarkable interest attaches to this communication because of its author and his connexion with the application of "the receptor analysis methods of Weil and Felix to the conception of a true cholera vibrio. Very great advances were made, but there is still disputation on the subject. One of the current dicta is now abandoned. Bruce White finds indisputable evidence of the transmutability of Ogawa and El Tor vibrios to Inaba vibrios by "focusing the serous influence" on the type-specific O antigen with the use of strictly monospecific antisera. Thus he establishes the fact that "the types are not separate species or subspecies but phases of a single species" and describes this first

also as "something like the specific and non-specific phases of the Salmonella. At the same time he expresses agreement with the view reached by Sir John Taylor on the collected results from an attempt to classify 311 vibrio strains, inagglutinable with O group 1 serum, that "with one possible exception, no case for the cholorigenic activity of any of these could be made out"

W. F. Harvey

GOTIAR, M. A. Isolation of the Cholera Vibrio. *J. Trop. Med. & Hyg.* 1948 Mar. v 51 No. 3 59-60 1 fig

Two labour-saving methods for speedy isolation of the cholera vibrio in times of epidemic are here described. The first requires a 25 ml. conical flask filled with alkaline peptone water to the bottom of its neck thus giving a concentration within a small surface area of the strongly aerobic vibrio growing rapidly from the faeces inoculum. Growth is taken from this surface to a semi-sloped mannito Andrade agar to which has been added about 1 ml. peptone water thus providing a composite stab slope and peptone water culture. The second improved method, especially useful for examination of convalescents or carriers omits the preliminary enrichment and selection. The faecal matter or vomit, is inoculated into a wide tube 3 cm. in diameter containing 0.5 per cent. agar dissolved in alkaline peptone water in which a piece of glass tubing about 6 cm. in length and 3 mm. in diameter is immersed. The medium rises in the small tube and is to be covered by about 5 mm. height of alkaline peptone water. After inoculation of the large tube, its surface is covered with a thin layer of sterile liquid paraffin to seal it. In this method advantage is obviously taken "of the active motility and strongly aerobic character of the cholera vibrios which" leads to their concentration in the only part exposed to the air in the small immersed glass tube. The further examination is according to routine.

W. F. Harvey

GALLUT, J. Sur le mécanisme de la réaction du choléra-rouge. [Mechanism of the Cholera-red Reaction.] *A. n. Inst. Pasteur* 1948, Jan. v 74 No. 1 27-39 5 figs. [11 refs.]

Those who would follow the argument presented should read Gallut on the utilization of glucose by the cholera vibrio [this *Bulletin* 1947 v 44 650 and 1948, v 45 177] as well as the work of Sax and his fellow workers (*ibid.* 1947 v 44 209). The essence of the cholera red reaction is the ability of the cholera vibrio to transform nitrates and to produce indole from peptone. As the production of nitrites is practically independent of the method of culture the variation in positiveness of the colour reaction must be based on the conditions for development of indole, except that the colour quality is conditioned by the nitrite indole ratio orange for a value greater than 1 red ("solferino") for a value between 1 and 2 and violet if greater than 2, when the concentration of indole is more than 50 mgm. per litre. Apart from these facts and the fact that in a glucose medium the production of indole and therefore the cholera red reaction is independent of the oxidation-reduction potential, we have to consider especially the part played by glucose in the reaction. In the total absence of glucose it is a simple reaction. If glucose is present the reaction demands its complete combustion, as distinct from fermentation products, activity fatal to the vibrio before it can be manifest. Moreover there are certain limits of concentration of the glucose within which the reaction can take place and which provide the time-table conditions for its optimum appearance. Other factors which come into play are those of anaerobiosis, aerobiosis and aeration of the medium.

W. F. Harvey

PASRICHA, C L, PAUL, B M, DAS GUPTA, A C & DAS, A K **Sulphasuxidine in the Treatment of Cholera** *Indian Med Gaz* 1947, Nov, v 82, No 11, 657

"Sulphasuxidine in the dosage used had no effect in reducing the mortality in cholera No untoward effects were noted in cholera cases after its use"

PASRICHA, C L, PAUL, B M, DAS GUPTA, A C & DAS, A K **Phthalylsulphathiazole in the Treatment of Cholera** *Indian Med Gaz* 1947, Nov, v 82, No 11, 656-7

"Although the death rate (7.3 per cent) is less in the phthalylsulphathiazole series than in the control series (10.1 per cent) the difference is not significant"

I BHATNAGAR, S S, DE SA, J, FERNANDES, F & DIVEKAR, P V **Chemotherapy of Cholera with a New Sulphonamide Compound ("6257")** *Laboratory Investigations and Field Trials* *Brit Med J* 1948, Apr 17, 719-23 [15 refs]

II. BRITISH MED, J 1948, Apr 17, 738-9 **The Chemotherapy of Cholera**

I Sulphaguanidine has been used in the treatment of cholera, but has not been conspicuously successful even where it was combined with hypertonic saline. Now the prospect appears of direct therapy with a new sulphonamide compound, which differs from the older compounds in not being a substitution derivative of sulphanilamide but a condensation formed by the molecular combination of two compounds, sulphathiazole and formaldehyde. Laboratory investigation showed that this preparation was markedly bactericidal and inhibitory. Animal experiments were carried out on mice and these involved both pre-infectious and post-infectious therapy, of 40 mgm daily for 4 days in the latter case, with groups of 20 animals each for intraperitoneal and subcutaneous routes. The test intraperitoneal dose of virulent *Inaba* vibrios did not exceed 2 MLD so as not to kill animals by toxic effect and the protection reached 100 per cent. Oral therapy in the experimental animals was not so effective and saved only 20 per cent, while the control group mortality was 100 per cent. The drug, owing to its low solubility in water, was given as a 20 per cent suspension in 2 per cent gum arabic. Absorption and excretion are both slow so that it is easy to maintain a long and effective blood concentration. In the field so far as first trials have gone, results are very satisfactory with the extraordinary saving of 82 patients out of 85 treated. Moreover "the patients were treated in their homes without the benefit of nursing and general medical care and no complementary treatment was resorted to". One advantage of treatment at home was, of course, the saving of an exhausting journey to hospital. The authors rightly stress that control of an epidemic of cholera by 7 days of therapy, producing complete freedom of the stools from infective vibrios is an event of major importance. That applies also to the use of the drug prophylactically in carriers who, if treated before panic or pilgrimage dispersal occurs may be rendered harmless. The average amount given over 7 days was 16 gm for a child, 23 gm for a woman and 25-30 gm for a man.

In one important respect the field trials differed from the animal experimentation in that administration was more successful by the oral route than by subcutaneous inoculation. No appreciable toxic effects were observed even with a 50 gm dose if cholera vomiting was extreme the drug was given.

The cyclical development of the spirochaeta in lice was observed in seven experiments and in the last four the same strain was transmitted through four successive batches of lice. The lice were infective the day after their infective meal, but were negative on the 3rd, 4th and 6th days, but positive on the 5th and 7th. No actual spirochaetes were seen in these lice and proof of infection depended on animal experiments.

The authors are of the opinion that the infections produced by lice during the first 10 days after an infective feed are caused by the organism in an invisible phase.

The cycle of *S. duttoni* in the louse seems to differ from that of the East African strain of *S. recurrentis* as the latter shows a more definite negative phase. [See this *Bulletin*, 1948, v 45 88.] In both, however, the negative cycle is terminated by the appearance of slender cork-screw-shaped metacyclic forms about the 15th day.

The course of the louse-transmitted *S. duttoni* infection in monkeys, mice and a rat and a hedgehog is given in tabular form. The results show that in pathogenicity it resembles the tick transmitted infection. Moreover, the results of cross-immunity tests clearly indicated that the infection in animals after the fourth transmission by means of lice, was serologically identical with the ordinary strain of *S. duttoni* and distinct from *S. recurrentis*.

E. H. Ellis

Naser, L. A. Sterile Splenic Abscess after Relapsing Fever. *Lancet*, 1948, Apr 10 555-8, 3 figs.

This paper is based on 7 cases admitted to the Hase El-Nay Hospital, Cairo between April and June 1946, during the decline of the epidemic of relapsing fever which attacked Upper Egypt during the winter of 1945-1946. Splenic abscess in relapsing fever is a rarity. EL RAMLY [this *Bulletin*, 1948, v 45 185] finding only 23 instances in 340 consecutive cases treated during the epidemic (1945-1946) of 139 fatal cases, splenic infections were found at necropsy in 23, of which 16 showed abscess formation.

In the present series, 4 were males and 3 females, and all gave a history of relapsing fever. The 3 females had had neosarsphenamine (2 or 3 injections, dose not stated).

The condition began with sudden pain, usually, described as severe, under the left costal margin in some cases referred to the left shoulder or epigastrium and usually subsiding without treatment.

In all cases there was an interval, after the pain had subsided, before abdominal swelling was noticed, and it was only after this mass had become very large that medical advice was sought. One patient sought aid for cough and pain in the chest, at a time when no mass was palpable in the abdomen. This developed in three weeks after the onset of pain. Where no chest complications were present there was no change in general health pulse or temperature but where the chest was involved the patient had fever dyspnoea raised pulse and toxæmia.

The liver was enlarged and tender in most cases. The splenic enlargement differed from the usual type in that (1) it did not move on respiration, but was firmly fixed (2) its borders were rounded and a nuch was felt in one case only (3) it was cystic and was tender in the early stages (4) in one case there was shifting dullness in the spleen (5) Traube's area was dull even in cases with no left pleural effusion. The size of the spleen varied the smallest reaching a finger breadth above the umbilicus, the largest nearly to the right iliac fossa.

Pleural effusion was present in 2 cases when they were first seen, the effusion in both being sterile and requiring repeated aspirations. Some of the early cases were misdiagnosed as retroperitoneal sarcoma, renal tumour, etc. One patient was first seen still complaining of the initial pain without enlargement of the spleen and the case was mistaken for pleurisy with effusion. Radiography always showed a raised immobile left dome of the diaphragm.

No malaria or relapsing fever parasites were found and, apart from one case of secondary infection, there was no rise in the polymorphonuclear leucocytes, even with a high leucocyte count. The Wassermann reaction was positive in the 4 cases where it was tested.

In the earlier cases, penicillin or sulphadiazine or both were given before operation, with no apparent good result. Splenectomy was not attempted in any cases owing to the dense adhesions and fixation of the mass, the abscess being drained through a separate left subcostal incision.

Unless secondary infection is present, penicillin and sulphonamides are not required and in early cases simple drainage results in cure. Post-operative complications were (1) left pneumonia followed by empyema, and (2) secondary infection from the operation sinus.

The spleen was transformed into a large sac with a dense fibrous wall, a rim of spleen tissue being found at the lower pole which was free. The abscess cavity was usually single and lined with shreddy necrotic tissue. The liver was enlarged and in some cases very congested.

The pus was odourless and usually a dull greenish-yellow colour, viscid and slimy. It was sterile in 6 cases in 1 case *Staph aureus* was found. Early lesions showed much necrosis and aseptic suppuration compatible with the formation of a sterile abscess but not hitherto described in relation to relapsing fever. [This complication must be a very rare one.]

ORTUZAR R, Pozo, S & ROSATI, S. Sodoku, septicemia a estreptococo moniliforme y fiebre de Haver Hill. [Sodoku, Streptococcus moniliformis Septicaemia and Haverhill Fever] Rev Med Chile 1947 Dec v 75, No 12, 774-S, 2 figs

This is another attempt at solving the problem of rat-bite fevers, Haverhill fever and that produced by *Streptobacillus moniliformis*. There is no little obscurity regarding these conditions. Sodoku is known to be due to *Spirillum minus* (*Spirochaeta morsus muris*), Haverhill fever is regarded as a form of rat-bite fever but the spirillum is not found and *Streptobacillus moniliformis* can be cultivated. On the other hand cases of Haverhill fever are recorded in which rats or rat-bites cannot be incriminated [see this Bulletin, 1942, v 39, 693]. A full table giving the distinctive characters of sodoku and rat-bite Haverhill fever is reproduced in this group namely, sodoku, a septicemia due to *Streptobacillus moniliformis* inoculated by the bite of a rat, and Haverhill fever due to the same organism but conveyed by contaminated food and not by rats and they give in the accompanying table the distinguishing features. [Since Haverhill fever has been shown in some cases at least to be due to rat-bite it seems incorrect to restrict the name as the authors have done to the syndrome unassociated with such a history. Would it not be better for the present at all events to discard the name Haverhill fever and divide the three under two main headings: fever due to *Spirillum minus* and diseases due to infection by *Streptobacillus moniliformis* and subdivide the latter into food?] food?]

	Sodoku	Septicæmia due to <i>Stryphobacillus moniliformis</i>	Flaverhill Fever
1. Causal agent	<i>Spirillum minus</i>	<i>Stryphobacillus moniliformis</i>	<i>Stryphobacillus moniliformis</i>
2. Mode of infection	Bite (rat)	Bite (rat)	Contaminated food
3. Incubation	1-3 weeks	1-3 days	2-8 days
4. Local changes and regional lymphadenitis	Marked	Slighter	Absent
5. Septicæmia	Moderate	Marked	Dominant
6. Cutaneous erythema	Marked; macular and papular	Marked; papular moniliform	Moniliform, petechial, polymorphous
7. Joint involvement	Absent	Commonly present	Usual features
8. Splenomegaly	Absent	Commonly present	Usual features
9. General adenopathy	Absent	Occasional	Frequent
10. Cyclic course	Absent	Frequent	Frequent
11. Haemoculture	Negative	Positive	Positive
12. Effect of Acetone	Good	Little or none	Little or none
13. Effect of Penicillin	Slight	Good	Good

Notes of 5 cases are given: one of sodoku, one of *S. moniliformis* septicæmia from rat-bite and resembling sodoku, one degenerated glandular form of Flaverhill fever, one with no history of rat-bite, one of epidemic arthritic erythema (Flaverhill fever) with general adenitis, and one of *S. moniliformis* septicæmia with valvular endocarditis associated with this organism and ending fatally.

II Harold Scott

NOURY M. Contribution à l'étude du sodoku et recherche sur l'action du sérum antispirelle. (Contribution to the Study of Rat-Bite Fever and Research on the Action of Anti-spirillum Serum.) Bull. Soc. Path. Exot. 1947 v. 40 Nos. 11/12, 430-35

Immune serum was prepared by inoculating sheep over a period of 14 months with blood and emulsions of liver and spleen taken from guinea-pigs infected with *Spirillum minus*. Spirilla were never found on macroscopical examination of the sheep's blood but the organism could be demonstrated by subinoculation of guinea-pigs or mice.

The lytic action of the serum *in vitro* was examined in 3 tests:

(1) 1.0 ml. amounts of a 1:5 dilution of blood from guinea-pig heavily infected with *S. minus* were mixed with undiluted serum in quantities from 9 to 2 ml. The mixtures and control containing 9 ml. of normal saline were incubated for 2 hours at 35°C. Doses of 1 ml. were inoculated into guinea-pigs, 3 being used for each dilution.

(2) 2 ml. of a similar 1:5 blood suspension were mixed with 16 to 0 ml. serum, incubated 2 hours at 35°C and made up to 40 ml. with normal saline. Again 3 guinea-pigs were inoculated from each dilution.



The control animals died in every case, but not a single guinea pig which received the mixtures containing serum, showing that the antiserum had completely inhibited the spirillum

(3) The infected material in this case consisted of a mixture of blood and emulsion of liver and spleen. Volumes from 9.9 to 80 ml were mixed with antiserum in amounts to give a final volume of 10 ml (0.1-2 ml serum), and incubated as before. In this test, 2 guinea pigs were inoculated from each dilution. The controls died, but the results of the serum mixtures were indefinite. Most of the animals became infected after long incubation periods, showing that the serum had only retarded the development of disease.

Serum from normal sheep and from syphilitic patients had no inhibitory action. The effect is therefore specific to anti-spirillum serum.

Prophylaxis was tried by injecting serum [dose not given] into guinea pigs 2-4 days before infection. No protection was obtained. Attempted treatment of infected animals with serum was also ineffective.

J C Brook

## LEPROSY

CHAUSSINAND, R. Sexe et lèpre [Sex and Leprosy] *Internat J Leprosy*  
Cleveland, Ohio 1947 Oct-Dec, v 15, No 4, 406-16

This is a careful survey of the question, based on extensive data and it brings out some new points. The author found 75.5 per cent of 1,002 cases to be in males, in accordance with general experience. Age curves show little difference in the first decade and after the 45th year, and the greatest preponderance of males between the ages of 15-20, this is attributed to a much larger number of males who contract the disease outside their families owing to great promiscuity in the course of their work and to greater susceptibility attributable to endocrine differences. In another table, 4-5 years are allowed for the incubation period and the probable dates of contamination in the two sexes are shown for each five-yearly period. The curves of these data show that up to the age of 15 there was a slightly higher percentage of infections among female children, after which the percentages fall in both sexes but more rapidly in females who are less exposed to extrafamilial infections. The curve of females also shows slight rises between 25-29 and 40-44, that is, during the period of most active gestations and at the commencement of the menopause, which somewhat increase the susceptibility of females, and are indications of the influence of endocrines. The benign nerve form is rather more frequent among females, and another table and curves of the age, sex and type on admission show a preponderance of the nerve form in males up to the age of 9, and a very large one in females of 40 and upwards. On the other hand, the lepromatous form is much more prevalent among females up to 29 and in males over 39 years of age. Thus, in general, the evolution is more serious in males, and females show more resistance except at an early age and during the period of gestation. All the data are based on experience in Cochinchina.

L Rogers

HARBITZ, F. Lepraforsting i Norge gjennom hundre år [Leprosy in Norway during a Century] *Nordisk Med* 1948, Apr 2, v 38, No 14, 677-9

The English summary appended to the paper is as follows —  
"This centenary address gives a survey of Norwegian contributions to leprology the great descriptive paper by DANIELSSON & BOECK published in



Ross, C M Some Differences in the Leprosy of the Gambia and Nigeria  
*Leprosy Review* 1948, Jan, v 19, No 1, 12-14

This note is based on a survey of 17,000 Gambia people in three areas extending up the river, with much lower humidity in the inland areas. The social conditions and diet are poor, meat is rarely eaten, and vitamin B is deficient. Eye lesions and rickets are common. Clinical and bacteriological examinations were made in all suspected cases. The percentages of different types were: lepromatous 13.5 per cent, tuberculoid 71.0 per cent, and unclassified 15.5 per cent. As compared with experience in Nigeria, lepromatous nodules were larger and they were present on the mucous membranes. In tuberculoid cases, a greater proportion showed erythematous reacting conditions. In a young female, small tuberculoid macules half encircling her body had the distribution of herpes zoster. The lepra bacilli in slides were relatively more numerous in each of the three types than in Nigeria, and scantily positive slides were astoundingly common in tuberculoid cases as compared with the negative results found in the Owerri Province of South Nigeria, and 19 to 40 per cent of tuberculoid cases were thus scantily positive. Unclassified cases showed 85 per cent to be positive. Nerve involvement was also more frequent. The highest incidence was found in the vitamin deficient upper river area, and the lowest at the mouth of the river where there were better conditions as regards vitamins and social aspects.

L Rogers

Ryrie, G V Regional Differences in Leprosy. Leprosy among Chinese in Malaya. *Leprosy Review* 1948, Jan, v 19, No 1, 4-11. 1 graph

This is an interesting comparison between the types of leprosy seen among Chinese, Malays and Indians in Malaya based on a large experience.

The disease is most virulent among Chinese and least so among Indians, three-fourths of the cases among the latter being of mild tuberculoid disease with a tendency to self-healing, but among the Chinese only one-third are of the tuberculoid type. The climate of Malaya is of the hot humid type, in which leprosy flourishes. On the other hand, a higher standard of living than in India tends to hinder the spread of the disease. The age incidence is important. Among the Chinese early macules are commonly found in children of 5 to 15 years of age, most of which tend to clear up, but in about one fourth tuberculoid lesions develop and may go on to the lepromatous condition, especially if the onset of the tuberculoid stage occurs early. When a reliable history is obtained in Chinese, in nearly every lepromatous case a tuberculoid stage was first observed, commonly in the age group 16-40. In a smaller number of persons of over 40 years of age, the proportion of tuberculoid cases is very much higher, but the tendency to become lepromatous is very much less. Major tuberculoid cases are more liable than minor to become lepromatous, but nerve thickening in tuberculoid leprosy is less evident in Chinese than in Indians, and it is rare in children and in those over 40. In view of the foregoing peculiarity of the evolution of leprosy in tuberculoid cases in Chinese subjects, active treatment is necessary, in order to prevent them becoming lepromatous. For this purpose, intradermal injections are of little value and they tend to obscure any evolutionary changes. Hydnicarpus oil or esters (deep subcutaneous injections) should therefore be pushed to the limit of tolerance in doses of 1 cc per 10 pounds body weight twice weekly, or 30 cc per week, for a patient of 150 lbs as a minimum, and increased by at least fifty per cent in acute or reacting cases, when improvement may be expected within three months. Some years' experience of this intensive treatment as compared with weekly injections of 1-5 cc has shown much more marked improvement and much less incidence of

used together with healthy control subjects and the reactions to intradermal injections of the antigens were noted after 24 and 48 hours and at the third week for early and late appearances, illustrations of which are recorded. The results showed that the three oily suspensions of *Mycob. leprae* antigens produced intense local reaction in 24 to 48 hours in all cases of leprosy including the lepromatous type, but they were most intense in tuberculoid cases. As early reactions were as constant, although less severe, with oily suspensions of typhoid bacilli they are not considered to be specific. Control tests showed that the early reactions are not due to the oily vehicles used, so the intense reaction in tuberculoid cases indicates that action of *Mycob. leprae* is increased in an oily suspension. The authors therefore think that the oily vehicle maintains contact of the bacilli with the dermis at the site of injection. Late reactions in tuberculoid cases were intense with hard infiltration and sometimes ulceration. In lepromatous cases a non-inflammatory nodule or plaque persisted, well localized and never ulcerating. In persons considered non-leprosy, infiltrated nodules or plaques with at times central areas of necrosis, were seen but less intense than in tuberculoid forms. A further interesting observation was that in several lepromatous cases intradermal injection of the oily suspensions of *Mycob. leprae* were followed after three to five months by pusill reactions to standard lepromin, but this change in the allergic state lasted for only a short time, after which lepromin again gave negative results. This temporary sensitization to lepromin is being further studied.

L. Rogers

DHARMENDRA. The Lepromin Test—A Review. *Lep. Hyg. Review* 1947 Oct. v 18, No 4 92-126 1 coloured pl. (99 refs.)

This is in itself a comprehensive summary of the literature of the subject with full references and quotations of the most important data on its various aspects from the first intracutaneous injections of lepra bacilli by MITSUDA in 1916. The advances made by HAYASHI in 1933 the suggestion of FERNANDEZ that the early and late reactions may be due to different antigens, and the explanation furnished by Dharmendra himself that protein constituents account for both reactions (the delayed one being, due to slow breaking up of the injected whole dead lepra bacilli in the tissues) are well brought out. Findings are quoted which indicate that the test was of considerable value in classification of cases, and in prognosis but little in diagnosis and treatment. Among matters regarding which there is still much difference of opinion may be mentioned the significance of occasional reactions in healthy subjects and in contacts of infected cases—claims that repeated tests may increase the resisting powers of children to infection—stronger reactions in summer than in winter—variations in reactions in different skin areas—and the effect of debilitating conditions in reducing reactions—all of these require further investigation. A careful discussion on the nature of the reaction leads the author to the conclusion that a positive lepromin reaction is an allergic phenomenon. Another use of the test is to determine if a given acid-fast bacillus is that of lepra or some other form for infection—the latter give positive reactions in lepromatous as well as in other types of leprosy which *Mycob. leprae* does not. This useful publication should be kept at hand for reference by all using the lepromin test the results of which are illustrated by a coloured plate.]

L. R. S.

IGNACIO J. L. & TIONG J. O. Further Observations on the Mitsuda (Lepromin) Reaction in Leprous Children. *Monthly Bul. Bureau of Health Manila* 1947 Feb-Mar v 23 No. 2, 83-101

This paper confirms the work of LARA (this Bulletin 1940) 37 632 on a tendency of young children to react more strongly to lepromin with increasing

age and with repeated tests. Three groups of children, amounting to a total of 216, were tested with lepromin, the results are tabulated and discussed. The greater proportion of strong reactors in those tested several times, compared with those injected with lepromin only once or twice, is noteworthy. Direct relationship between repeated testing and clinical improvement or subsidence of leprotic lesions indicates a favourable influence of the lepromin in children and may indicate that lepromin has some immunizing value, especially when the subjects are of about the same age, but further work is required to establish such an effect. Further, in 31.5 per cent of first injections the original lesions had apparently already healed which indicates increased natural resistance after childhood, as is believed to be the case with tuberculous children. Strong reactions probably indicate a relatively high degree of resistance with a better prognosis, but the relationship is not constant. Children showing consistently weak reactions also have a poor prognosis, but they form a small minority of the cases. These observations confirm the prognostic value of lepromin reactions. L Rogers

NOLASCO, J O. The Potency of Stored Lepromin. *Monthly Bull Bureau of Health* Manila 1947, Feb-Mar, v 23, No 2, 103-14

Quotations from medical literature show very varying opinions on the keeping powers of lepromin so this paper is timely. The lepromin used in the present investigation was prepared by the technique of Hayashi, and was proved by microscopical examination to contain numerous well-preserved lepra bacilli, some in globi but as the number may vary much in different specimens, this method of preparation is capable of improvement. In the first series of tests before the Japanese invasion of the Philippines eight lepromins, which had been stored for 1 to 41 months in a refrigerator, were all injected in the forearms of twenty patients and weekly observations were made up to the 28th day, these are discussed in detail. Except for some minor variations in the reactions following the use of particular samples, all gave normal reactions with ultimate suppuration of the nodules at the sites of injection. In a second series, seven specimens kept throughout the war, with only very occasional refrigeration for a few hours, up to periods of 49 to 96 months, together with a control only 14 days old were injected simultaneously in another group of twenty patients. Microscopical examinations showed undiminished numbers of lepra bacilli in all the specimens, and once more the reactions were typical. The author therefore concludes that lepromin prepared by the Hayashi-Mitsuda method keeps its properties undiminished for very long periods without any necessity for its being preserved in a refrigerator. L Rogers

DE SOUZA LIMA L & DE SOUZA CAMPOS, N. *Lepra tuberculolde* Estudo clinico histopatológico. This book is reviewed on p 658

WOLCOTT R R. Erythema Nodosum in Leprosy. *Internat J Leprosy* Cleveland, Ohio 1947, Oct-Dec v 15, No 4, 380-88, 4 figs (1 on pl)

The author states that erythema nodosum occurring in leprosy is often confused with acute lepra reactions and he gives the following points of differentiation between the two conditions. Erythema nodosum differs from the acute lepra reaction in that its onset is less abrupt the numerous evanescent discrete red nodules rarely show lepra bacilli, fever may be absent or intermittent, and without loss of weight and strength. Moreover, the lesions of erythema nodosum are painful on pressure, show vascular changes and are common under

sulphone treatment, during which lepra reactions are rare. Very numerous nodules may appear within a few hours, and fresh lesions may occur when the first have subsided. Oedema of the corium with swollen connective tissue fibres are found microscopically and the appearances indicate an antigen-antibody immune reaction. There is a close relationship to treatment, for only 7 per cent. occurred before treatment was begun, but they were more frequent under sulphone treatment and also of shorter duration and their appearance is considered to be a definite indication of the resistance of the host. Intramuscular injections of Fousidin in 3-5 cc. doses produced general improvement after a few days, and this allowed antileproous treatment to be continued without interruption in nearly all the cases especially when sulphones were being used.

L. Rogers

ROGERS, L. Combined Chaulmoogra and Sulphone Treatment of Leprosy and Tuberculosis. *Lancet*. 1948, Apr 3 515-17 [14 refs.]

LANCET 1948, Apr 3 524 Chemotherapy of Leprosy

Oral administration of chaulmoogra oil in the past was so nauseating that few leprous patients could be induced to persevere with it. Great advance therefore was made when its active constituent sodium hydnocarpate Alepol which was given by injection, was substituted. The author in 1916 demonstrated that subcutaneous injection of alepol led to the breaking up of the bacilli sometimes with softening of nodules, and, later that, when intravenously injected, it produced more rapid destruction of the bacilli and more rapid improvement in the lesions. But intravenous injections in all cases might result in long-continued fever and debility although the clearing up of lesions might be remarkable. The author therefore proposed that injections should be given intramuscularly for some weeks and, when progress began to slow down, the intravenous route should be used for a few doses. The mode of action of the drug was found to be by its fat-solubility property and by breaking down the protective fatty envelope of the bacilli and rendering them vulnerable.

In recent years, sulphone preparations have been used in treatment of leprosy and favourably reported upon, especially Promin by PAGET *et al.* (this Bulletin 1947 v. 44 594) in the Carville leprosarium, and Promizole and Diasone by the same workers and by MUIR (*ibid.* 326 327). The latter drugs have the advantage of oral administration, whereas the first must be injected. These drugs act by destroying the bacilli entering the blood-stream, so that fresh lesions by blood transmission are prevented.

The author has shown thus that the actions of chaulmoogra and these sulphones are complementary the former destroying the bacilli in large numbers in the leprous lesions with the risk of surviving organisms being disseminated by the blood, whereas the latter destroy them when they reach the circulation. In order to ensure the presence of the bactericidal drug in the blood before pushing the chaulmoogras to the point of softening of the lesions and dispersion of organisms, it is recommended, says the author that several weeks' treatment with one of the sulphones should precede the larger doses of chaulmoogra.

Analogies between *Myra lepras* and *Myra tuberculosis* have naturally led to the suggestion of using sodium hydnocarpate and morrhuate in tuberculosis, and success has followed the use of colloidal copper morrhuate *Gadum*, in this disease the author suggests that trial should be made of this in combination with sulphones or with streptomycin in tuberculosis on the same principles as in leprosy."

A leading article on this subject points out that the actual evidence of chaulmoogra preparations being bacteriolytic is not strong and that their effect may be due to counter-irritation and the stimulation of a tissue response. The article also refers to untoward and possibly dangerous side-effects of treatment with sulphones, such as gastro-intestinal disturbance, haemolytic anaemia, haematuria and even agranulocytosis. It is suggested, further, that *p*-aminosalicylic acid, which seems to have some specific action on acid-fast bacilli, has low toxicity and has been tried in tuberculosis, might, when it is more readily available, be given a trial in leprosy.

FAGET, G H & ERICKSON, P T *Chemotherapy of Leprosy* *J Amer Med Ass* 1948 Feb 14, v 136, No 7, 451-6, 6 figs [Refs in footnotes] H Harold Scott

This paper records the latest observations on the sulphone treatment of leprosy. This group of drugs has now been under trial in lepromatous cases at the Carville Settlement, U S A, for six years, almost entirely with better results than any former treatment. Promin on account of its toxicity has to be given intravenously in doses gradually increased from 1 to 5 gm daily for two weeks at a time, with one week's interval at the end of each fortnight. Diasone is given orally, beginning with 0.3 gm in a capsule or as a tablet daily, and increased if well tolerated to two or three such doses daily, with periods of two weeks' rest after every two months' treatment. Promizole is given orally 0.5 to 1 gm three times daily and gradually increased to the optimum dose of 6 to 8 gm a day. No renal damage was found from any of them under the carefully controlled conditions of medication, but careful watch must be kept for anaemia or leucopenia, which may require temporary cessation of the treatment and the use of iron or liver therapy.

Most of the patients treated had advanced lepromatous disease notes and illustrations before and after treatment of three cases show striking improvement. Progress is seldom evident in less than six months and is very slow, but steady with very few relapses and is in proportion to the duration of treatment. Promin and diasone give very similar results. Of the patients treated, 25 per cent show improvement after six months, 60 per cent after one year, 75 per cent after two years and almost 100 per cent after three years' treatment. It is shown by slow shrinking and absorption of nodules until only a pigmented scar may remain, ulcers develop healthy granulations and heal and there may be some regrowth of hair. Mucous lesions respond better than cutaneous lesions. The frequency and severity of reactions are reduced. *Lepra bacilli* in the lesions gradually become less numerous and after four years they disappear in over 50 per cent. Those entering the blood stream are eliminated and the development of fresh lesions is prevented. The histological changes in lesions are of an atrophic nature. The proportion of cases in which the disease is arrested under prolonged promin and diasone treatment is 83 per cent in 1-2 years, increasing to 21 to 29 per cent after three to six years. Antibiotics have also been tried in leprosy, but penicillin is only of use in secondary infections of ulcers. Streptomycin has given encouraging results, but they are not as yet conclusively demonstrated and require further tests. In a discussion on the above paper, H M Johnson of Honolulu reported encouraging results in Hawaii from the use of promin and diasone. L Rogers

JOHANSEN F A & ERICKSON, P T *Promizole Treatment of Leprosy* (A Progress Report) *Internat J Leprosy* Cleveland, Ohio 1947, Oct - Dec v 15 No 4 378-9

This note records a trial lasting two and a half years of Promizole in leprosy at the Carville Leprosarium U S A. It was found to be slightly less toxic than

the other sulphonates but does not appear to have any other advantages. It is given orally in doses six to eight times as great as those of promin or thiazone and becomes distasteful and unpalatable. It also produces a harmless cherry red colour of the urine. It is synthesized with difficulty and is expensive. Treatment was started on 25 patients, who have fallen to 15 of whom 7 have been under treatment for 2½ years, but two of these are now using other preparations. Two of the patients have become negative bacteriologically and clinical improvement continues to take place. Of 5 patients treated for only one year all are still bacteriologically positive. Three of the patients have died of intercurrent diseases. In view of these drawbacks it is not proposed to continue the trials after the present supplies of promizole are exhausted.

L. Rogers

DE MESQUITA A. P. Scabra's Photo-Oxidase Test in Leprosy. *Med. Times*, New York, 1948, Feb., v 78 No. 2, 56-60 73 4 figs.

This paper describes a new prognostic test of a technical nature. Scabra has studied oxidases and worked out an index for them in the leucocytes, which varies with barometric pressure and a photo-oxidase test for measuring them. The erythrocyte oxidase falls in tuberculous subjects and this is due to "Factor P" secreted by tubercle bacilli inactivating the hase produced by the lymphocytes. Scabra also found a similar drop in erythrocyte oxidase in a few cases of leprosy. This test has now been applied in 100 leprosy cases, with the result that the lowest readings are found in the more serious cases with the worst prognosis, mainly lepromatous disease in which it is below the normal limit of 40. In nerve cases classed by the South American nomenclature as "neurocharacteristic" and tuberculoid on the other hand, the readings are usually above 40. Thus among 57 lepromatous cases, Scabra's photo-oxidase tests showed low figures in 53 (79 per cent.) Of 14 cases without low readings, 6 have greatly improved and 8 have become free of cutaneous signs. The nerve types revealed normal readings over 40 in 25 of 33 cases (75-76 per cent.) and several of the exceptions were not doing well. A table and illustration show the readings in the 100 cases. For technical details, the original should be consulted.

L. Rogers

## HELMINTHIASIS

THIERY C & THIBAUT C. *Bacillus bifi* dans la lutte contre les helminthes intestinaux de la souris. [*Bacillus bifi* as an Antagonist to Intestinal Helminths in Mice. *C. R. Soc. Biol.* 1948, Jan v 142, No. 12, 44-6 2 graphs.

The following is a translation of the author's summary.

The use of a culture of *Bacillus bifi* in the form of washings provides a powerful weapon against intestinal helminths in mice and is completely innocuous for the host. A hope is expressed that it will be possible to bring it into general use in human and veterinary medicine.

H. J. O. D. Burke-Gifford



- 1 KREIS, H A Eine systematische Bemerkung zur Arbeit H Vogel und W Minning Ueber die Einwirkung von Brech Weinstein, Fuadin und Emetin auf Bilharzia japonica und deren Eier im Kaninchenversuch [Comment on the Paper by Vogel and Minning on "The Action in Rabbits of Tartar Emetic, Fouadin and Emetine on *Schistosoma japonicum* and its Eggs"] *Acta Tropica* Basle 1947, v 4, No 3, 259-60
- 11 — Bilharzia oder Schistosoma ? Ergänzende Mitteilung zur Bemerkung H A Kreis in *Acta Tropica* Vol. 4, 259-260, 1947 [*Bilharzia* or *Schistosoma* ? Further Communication] *Ibid* 1948, v 5, No 1, 87-8

1 VOGEL and MINNING's paper was abstracted in this *Bulletin* [1948, v 45, 196] and the author of this comment does not criticize the work which he says is of much interest, but he objects to the name of the trematode. He traces historically the changes in the naming of this worm. Bilharz describing it in 1852 called it *Distomum haematobium*. Six years later, Weinland stated that it did not belong to this genus *Distomum* and put it under a new genus *Schistosoma*, and *Schistosoma haematobium* (Bilharz, 1852) became *S. haematobium* Weinland, 1858. But in the same year, Diesing gave it the generic name of *Gynaecophorus* and in 1859 Cobbold, in honour of its discoverer, called it *Bilharzia* and the same year Moquin-Tandon called the new genus *Thecosoma*. The author argues that as Weinland was the first to show that it did not belong to the genus *Distomum*, according to the laws of nomenclature its correct name is *Schistosoma*. VOGEL and MINNING, however, called the helminth they were dealing with *Bilharzia japonica* on the ground that Meckel used the term *Bilharzia* in 1856, or two years before Weinland created the genus *Schistosoma*. LEUCKART in his work on *Die Parasiten des Menschen* calls the urinary schistosome "*Bilharzia* Cobbold, 1859" which is certainly wrong if Meckel had called it so three years before. So far, all seems plain sailing, but prolonged search has failed to find where Meckel called it *Bilharzia*, and the works of Lutz, of Faust, of Worth, Martin, Hunter and others say nothing about Meckel. Therefore, until proof is obtained that Meckel *did* make the genus *Bilharzia* in 1856, the name *Schistosoma* Weinland, 1858 must hold good.

11 In his supplementary note Kreis dwells on the fact that in the account of SENN's booklet on Theodor Bilharz, Professor Leiper speaks of a posthumous work "Mikrogeologie" by Meckel von Hemsbach, published in 1856, in which the generic name *Bilharzia* is used. Meckel as the originator of the name *Bilharzia* is also mentioned in a book on *Famous Tropical Physicians* by G. OLPP published in Munich in 1932. In Professor Leiper's words "Those who regretted the displacement of the generic name *Bilharzia* Cobbold, 1859 by *Schistosoma* Weinland, 1858 under the Law of Priority will rejoice in the restoration of *Bilharzia* Meckel, 1856 under the same Law" [See this *Bulletin*, 1932, v 29, 168]. In spite of, or in comment on, this, E W PRICE (*J Parasitology*, 1933-4, v 20, 111) wrote "but in this case priority is of little moment in view of the fact that in 1922 *Schistosoma* was placed on the list of official names under Opinion 77 of the International Commission on Zoological Nomenclature". To end the dilemma Dr Kreis in 1938 asked the Commission for a decision and he received a reply from the President saying that he would bring the request to the notice of the members, he suggested that in the meantime as *Bilharzia* could obviously claim priority, this name should be used and provisionally *Schistosoma* should be inserted in brackets. Dr Kreis says that he repeated his request in 1947, but, so far as he knows, no decision has yet been made. He adds naively, "When the decision is reached, it will be authoritative".

The present author with BLAIR treated seven patients with acriflavine in Salisbury Southern Rhodesia all suffered from *S. haematobium* infections and three had *S. mansoni* as well. The patients were adolescent school children and all were passing viable eggs. They were given the dose quoted by Fisher namely a total of 0.01 gm. per kgm. body weight in five equal daily doses of 2 per cent. acriflavine. No evidence of toxicity was noted.

At the end of treatment one patient with *S. haematobium* had ceased to pass viable eggs and remained negative for the further period of two months follow up. One month after treatment a patient who had *S. mansoni* was negative but showed eggs again after 2 months.

It is pointed out that most of Fisher's cases had become negative immediately after treatment and that, unlike the present instance his cases comprised solely intestinal schistosomiasis.

In the present author's small series of cases of vesical schistosomiasis, the effect of acriflavine was found to be almost negligible.

H. J. O'D. Burke-Gaffney

SCHUBERT M. Conditions for Drug Testing in Experimental Schistosomiasis *mansoni* in Mice. *Amer J Trop Med.* 1948, Jan. 23, No. 1: 1-26  
4 figs. [17 refs.]

An investigation is described to find the best method for testing drugs on experimental schistosomiasis. A number of points are involved (1) The prices of schistosome and its intermediate host. *S. mansoni* and *Australobius glabratus* were convenient and satisfactory. *S. haematobium* would develop well in mice but it was difficult to obtain any large number of cercariae from *Bulinus truncatus*. *S. japonicum* was not available. (2) The animal host chosen was the mouse. Hamsters develop infections more readily but are less easy to use for screening drugs. Rabbits are convenient if large numbers of adult worms are required. Rats are not very susceptible to infection, and are unsatisfactory. (3) The mice were infected by intraperitoneal injection of a standard number of cercariae. This was more convenient and uniform than immersing them in water containing cercariae. (4) The optimum number of cercariae per mouse was 100-150 when this number is injected intraperitoneally about 9 per cent develop into adult worms and 80 per cent of the mice are infected. Higher doses of cercariae kill too many of the mice. (5) Even with a standard dose of cercariae the number of worms which develop in the mice varies considerably. In groups of 15 mice there may be 5 or 20 worms in individual mice. (6) The infection in the mice becomes mature; eggs are passed, during the sixth or seventh week after infection. Treatment was therefore begun during the eighth week. There was no evidence of spontaneous cure of the mice during the first 38 weeks. (7) The drug was given daily for two weeks usually by intraperitoneal injection. If the drug was insoluble it was injected as a suspension or given in the diet. (8) The criterion of cure. Even after treatment with Fouadin or sodium antimony tartrate few of the mice become completely free from worms. Accordingly the effect may be judged by the location of the worms (antimonials drive them from the mesenteric mes into the liver) and by the percentage of worms paired (diminished by antimonials). The presence or absence of viable eggs in the faeces was found to be very variable even in untreated mice. (9) During the first two weeks after treatment worms which have been driven into the liver but not killed may recover and reascend the mesenteric mes and begin to lay eggs again. Accordingly the mice should be held for two weeks after treatment and then killed and the number and location of the worms should be compared with those of control untreated mice. Usually 10-15 mice are used in each group. The

author seems to have had more difficulty in demonstrating the helminthocidal action of active drugs than KIKUTH and GÖNNERT did in Germany, the latter workers have used a similar technique since 1936 and judged the response according to the passage of eggs and the presence or absence of living worms at autopsy 4 weeks after treatment ]

SCHUBERT, M Screening of Drugs in Experimental Schistosomiasis mansoni in Mice *Amer J Trop Med* 1948, Jan, v 28, No 1, 137-56

By means of the methods described above, over 400 compounds were tested, the names of these being given in lists According to their therapeutic effects, the drugs may be divided into four categories —

- (1) Drugs which cured most of the mice, viz antimony tri(2 naphthylethyl mercaptide), antimony tri(n-dodecyl-mercaptide), and n-butyl 3,4 antimonyl gallate
- (2) Drugs which killed some of the worms, viz Fouadin, antimony trithioglycollamide, antimonyl 2 mercaptothiazoline, antimony tri (2 mercaptoimiazogluconate, emetine, miracil.
- (3) Drugs which had only a slight action, viz sodium antimony tartrate and 32 other compounds
- (4) Drugs with no action

It should be noted that the pentavalent antimonials, neostibosan and neostam, both showed considerable activity and they probably deserve further clinical trials in the treatment of schistosomiasis Antimony compounds soluble in oil also seemed worth further clinical investigation Miracil was found to have considerable action when given in the maximum tolerated dose by injection or by mouth and it is said to deserve further investigation, however it was not so effective in the author's animals as it was in those of KIKUTH and GÖNNERT [This paper contains numerous data of great interest to those concerned in the search for new active compounds and should be consulted in the original ]

SCHUBERT M Effect of Drugs during Earliest Stages of Experimental Schistosomiasis mansoni in Mice *Amer J Trop Med* 1948, Jan, v 28, No 1, 157-62

Mice were infected with *S. mansoni* by the technique described above On the first five days after intraperitoneal injection of the cercariae they were treated with daily doses of drug by intraperitoneal injection, or the drug was given in the food The purpose was to prevent the development of the infection The mice were killed and examined after eight weeks Eighty drugs were tested in this way Seven showed significant protective action, viz antimony tri(2 naphthyl ethyl mercaptide), Fouadin, antimony tri (n-dodecyl mercaptide) neostam, neostibosan, urea stibamine and sodium antimony tartrate (in order of decreasing activity) The doses used were approximately the maximum tolerated ones Miracil showed very little activity

F Hawking

KUNTZ, R E, STIREWALT, M A & BUCHHEIT, J R Method for testing Ointments and Fabrics to determine their Effectiveness as Barriers to Schistosoma Cercariae *Amer J Trop Med* 1947, Nov v 27, No 6, 691-7, 4 figs [11 refs]

Control of schistosomiasis in war may be attempted by destruction of the snail hosts (only moderately successful hitherto), temporary elimination of

cercariae by cercaricidal substances or by protection of the skin by the use of uniforms made from protective fabric or the use of repellents or barrier substances. In tests on animals estimation of the penetrating power of cercariae by keeping the animals for 15-40 days and then dissecting them and counting the parasites which have developed is cumbersome and the authors have devised a shorter test which is probably sufficiently accurate. It is based on the observed fact that cercariae of *Schistosomium douglasi* and *Schistosoma mansoni* penetrate hamsters and white mice with equal facility and are affected to about the same extent by barrier substances. These animals show skin reactions when the cercariae have penetrated but certain white rabbits about 6 months old constantly show much more prominent reactions to cercariae of *S. douglasi* which render assessment of invasion much easier. It can be assumed, therefore, that the skin reaction due to *S. douglasi* is a reasonably accurate index of the invasive powers of equal numbers of cercariae of *S. mansoni* under the same conditions (but the authors do not prove that what is true of hamsters and mice is necessarily true of rabbits).

The authors describe a rubber belt containing four test chambers of glass tubing 1 inch in diameter which is applied to the skin of the belly of the rabbit. Into these chambers about 25 cercariae are introduced and left for 1 hour (with clothing barriers 50 cercariae are left for 1 hour) and the numbers of inflamed spots caused are counted every 4-8 hours for 2 days. The barrier ointments are placed on the skin before the cercariae are applied, but the fabrics are placed 1-3 mm. from the skin and the intervening space is filled with water—the cercariae are placed outside the fabrics.

For details of these procedures the original must be consulted. No results of actual tests are given. According to the list of references most of the work done on fabrics and barrier substances has been recorded in official reports.

Charles H. Welch

PERIGAN T. P. The Endemicity of *Schistosomiasis japonica* in Sorogon, Southwestern Luzon. *J. Philippine Med. Ass.* 1949 Jan., v. 24 No. 1 19-27 1 fig. & 1 map on pl.

The known endemic foci of *S. japonicum* infection in the Philippine Islands are Eastern Leyte, Samar, Surigao and Agusan especially around Lake Mainit and Mindoro near Lake Naujan. Another focus has recently been found in Western Lanao (see this *Bulletin* 1947 v. 44 832). The author has now confirmed a newly discovered endemic area in Sorogon, Luzon. He had observed a few patients in the Philippine General Hospital, who came from Sorogon, and he therefore made a survey in that area finding 25 infected persons most of whom had never left the district. A few of these persons were unaware of any serious illness, but in 16 the liver was enlarged, and distension of the superficial abdominal veins was found in 7. No less than 6 had had epileptiform attacks, but this should not be regarded as indicating the proportion so affected, since these patients were examined for schistosomiasis because they gave this history.

Search for snails revealed *Oncomelania quadrasi* in three streams out of many investigated. None of the snails was infected but there is little doubt that this species well known as the intermediate host elsewhere is responsible for spread here.

In addition to schistosomiasis the author found other infections in 113 of 114 persons examined including paragonimiasis and balantidiasis in one boy.

Charles Welch

JAHNES, W G & HODGES, E P An Improved Method of sedimenting *Schistosoma japonicum* and other Helminth Ova *J Parasitology* 1947, Dec, v 33, No 6, 483-6 [15 refs]

The authors tested a number of chemicals and reagents in a search for the most effective method of sedimenting eggs of *S japonicum*. A control method of evaluating the tests consisted in the use of 0.5 per cent of glycerine in tap water. Of all the materials employed, 10 per cent ethyl alcohol (sp gr 0.986) gave the best results, with the highest egg counts and no distortion. The procedure is as follows: 5 gm of stool are emulsified, strained through four layers of moistened gauze and allowed to sediment for 1 hour, 45 minutes and 30 minutes successively, decanting at each time interval and replacing with fresh solution. After the final sedimentation, 0.15 cc are taken from the top and bottom of the residual sediment, respectively, and examined.

HUNTER, G W, HODGES, E P, JAHNES, W G, DIAMOND, L S & INGALLS, J W, Jr *Studies on Schistosomiasis II Summary of Further Studies on Methods of Recovering Eggs of S japonicum from Stools* *Bull U S Army Med Dept* 1948, Feb, v 8, No 2, 128-31, 2 figs [Refs in foot-notes]

Previous studies described evaluation of the various laboratory methods available for diagnosing *S japonicum* infection [this *Bulletin*, 1947, v 44, 440]. The present paper makes further comparisons and indicates that two new methods have shown themselves to be superior to all others in current use.

In the comparisons, qualitative and semi-quantitative estimations were made of 10 techniques, with the use of stools of dogs infected with *S japonicum*, naturally infected human stools and those of monkeys infected with *S mansoni*. The techniques were (1) direct smear, (2) sedimentation, (3) hydrochloric acid, Triton NE, ether centrifugation, (4) hydrochloric acid, sodium sulphate, (5) sodium sulphate Triton NE, ether centrifugation, (6) sodium sulphate, ether, xylol, (7) funnel centrifugation, (8) AMS I method, (9) centrifugal sedimentation, now reported as the AMS III method, (10) a modification of the AMS II method, (10) a modification of the AMS I technique.

The AMS I technique was a modification of the Telemann hydrochloric acid and ether method as used by WELLER and DAMMIN [this *Bulletin*, 1947, v 44, 98] except that the hydrochloric acid was mixed with equal parts of sodium sulphate. The AMS II method modified the AMS I technique by using 2 gm of stool, by washing with water centrifugation before the HCl, sodium sulphate Triton NE, ether centrifugation technique and by swabbing out the tube before decanting the final residue on to a slide. The AMS III method substitutes washing 3 times with the HCl and sodium sulphate mixture instead of water before treatment by the HCl, sodium sulphate, Triton NE ether technique. The last named method is described in detail in the text. It requires less than 15 minutes. A total of 37 qualitative and 15 semi-quantitative comparisons were made. In every case, the AMS II and III proved to be the most satisfactory. The results are shown in two figures, which demonstrate strikingly only are more eggs revealed, but the slides are washed cleaner and are therefore comparatively easy to read. It is added that the AMS III technique also appears to be efficacious for the detection of other helminths, and has the advantage of detecting *S japonicum* eggs whether they are immature, mature or degenerate. It can also be used satisfactorily in examining stools of those who have already been treated.

H J O'D Burke-Gaffney

HUNT W. E. ABRAHAMSON W. & WEAVER, T. A. Jr. Cerebral Schistosomiasis. Report of a Case simulating Cerebral Neoplasm. *J Amer Med. Ass.* 1948 Mar 8, v 136 No. 10 688-9 8 figs. [Refs. in footnotes.]

A white labourer aged 35 years, served with the army in Leyte where he bathed in proscribed fresh water streams. In the United States in September 1946 he began to suffer from transient loss of motor and sensory function on the left side of the body and right sided headache on one occasion he lost consciousness during an attack. Changes in his personality were noticed by his wife. In November 1946 a diagnosis of brain tumour was made after electroencephalographic and ventriculographic examinations. At operation, scattered white milky nodules were seen on the right cerebral convolutions. In the posterior portion of the inferior frontal gyrus there was a nodule about 5 mm. in diameter which was removed. On section schistosome ova, surrounded by lymphocytes and eosinophiles, were found lying in an area of connective tissue proliferation containing Langhans-type giant cells. Repeated stool examinations, sigmoidoscopic scrapings and urine examinations failed to yield schistosome ova, but the patient was put on a course of antimony potassium tartrate. He made a good recovery but there was some residual weakness of the left arm and he suffered an abortive sensory seizure some five months after the operation and treatment. [See also this *Bull.* 1947 v 44 916.]

I R D Adams

CARROLL, D & HUNNINER, L. V. Studies on Schistosomiasis japonica in the Philippine Islands. 3. A Clinical Study of 72 Cases treated with Tartar Emetic. *Bull Johns Hopkins Hosp* 1948 Mar v 82, No. 3 346-72

The treatment of *S. japonicum* infections on Leyt in 1944-45 with Fouadin has already been reported (this *Bulletin* 1947 v 44 834). The present report deals with 72 patients treated with tartar emetic, 32 of whom were followed into their seventh month of illness.

All cases were primary infections in hitherto unexposed American soldiers. The incubation period averaged 50 days for 68 cases. Five cases were classified as severe 31 as moderately severe 32 as mild and 4 as asymptomatic.

In treatment 1.89 gm. of tartar emetic was used. The stock solution was 0.4 gm. of the drug per 100 cc. 1.5 per cent. dextrose in normal saline the solution was not heated and was used within 3 hours of being mixed.

The solution was given in graded doses intra-venously every other day for 18 doses, namely: 1st dose 0.020 gm. of tartar emetic (5 cc. of solution) 2nd, 0.040 gm. 3rd, 0.060 gm. 4th, 0.080 gm. and, after the fourth dose 0.120 gm. (30 cc. of solution) for all further doses.

In the first four doses the solution was diluted with the dextrose-saline to make 30 cc. of liquid injected. Injection was made into the antecubital vein over a period of about 10 minutes. Early minor reactions were cough, nausea and vomiting while in some patients stiffness of the joints developed later as more of the drug was given. A chart indicates that there were many minor reactions also in four cases tartar emetic had to be discontinued owing to purpura substernal pain ascular collapse and cough with diarrhoea and vomiting, respectively. One month after the course of tartar emetic was completed 32 patients were retreated with 40 cc. of Fouadin owing to the presence of degenerated eggs in their stools. The Fouadin was given intra-muscularly in doses of 5 cc. daily for 8 days.

All patients were discharged after 1 to 4 months. Few of them felt completely well, although they carried on light duty. Of 31 patients weighed 7 months later 35 per cent. had lost weight. There was no striking clinical

improvement with the institution of tartar emetic therapy After the third month, glandular enlargement was no longer appreciable, and the spleen and liver tended to remain palpable in only a minority of the patients These features are shown in a chart

Tabulated figures for leucocyte and eosinophile counts are given as time passed, these counts approached normal Sedimentation rates of 29 patients in the 7th month were normal

Two of the patients showed mature *S japonicum* eggs in the 16th week after tartar emetic treatment and 2 in the 17th week Three of these 4 had been retreated with Fouadin

In 8 of 32 patients in the 7th month, sigmoidoscopy showed nodules in the rectum or sigmoid Only one of these had a positive stool and 4 had been retreated with Fouadin

The authors found no significant difference between the cases which recurred and those which did not in regard to the original leucocytosis and eosinophilia or for these values at the end of seven months Retreatment with Fouadin was not effective in preventing recurrences None of the asymptomatic cases recurred. The impression was gained that patients having tartar emetic had fewer recurrences than a comparable group treated with Fouadin alone [*loc cit*]

H J O'D Burke-Gaffney

DOUGLAS D M Hydatid Disease *Edinburgh Med J* 1948 Feb v 55, No 2, 78-91, 4 figs

A general account with special reference to experience in Iraq

HOBSON, A D The Physiology and Cultivation in Artificial Media of Nematodes Parasitic in the Alimentary Tract of Animals *Parasitology* 1948, Feb, v 38, No 4, 183-227 [Numerous refs]

This is a detailed review of current knowledge of the physiology of the parasitic stages of nematode parasites in animals with particular reference to those species which are found in the alimentary canal, and of attempts which have been made to keep adult and larval phases of parasitic nematodes alive *in vitro*

The review is a very useful work for anyone interested in the subjects or about to undertake research in them, but of no immediate value to human medicine

J J C Buckley

KHOO, F Y & CHIANG, H-S Hookworm Disease showing Abnormal Roentgenologic Small Intestine Changes Three Case Reports *Chinese Med J Shanghai* 1947, Sept-Oct, v 65, Nos 9/10, 349-56, 4 figs on 2 pls

Since MACKIE [*Med Clin North America*, 1933, v 17, 165] drew attention to the radiological changes in the small intestine in non-tropical sprue, considerable attention has been paid to the radiological picture in tropical gastrointestinal disorders and malnutritional states

Golden has divided these changes into two main classes,

- (i) Changes in motility, hyper- and hypo-motility and -tonicity, abnormal segmentation, scattering effect, and gas and fluid levels, and
- (ii) Changes in the mucous membrane—exaggeration or obliteration of the mucosal folds

These changes are not pathognomonic of any particular condition, but occur in many nutritional disorders whether these are primary, or secondary to disease of the intestinal tract Worm infections are included amongst the latter

In 1943, KRAUSE and CRILLY [*this Bulletin*, 1944, v 41, 139], reporting on 97 cases of *Necator americanus* infection in white adult males, found in varying

species development is slow and somewhat irregular compared with what takes place in *C. salicis* and *C. dimidiata* in W. Africa.

Three hundred individuals of *C. distinctipennis* and *C. longicornis* were dissected after feeding on *Loa*-infected blood. Growth was slow and 18-20 days were required before the embryo reached the stage of full larval development. Out of 600 caught in the wild state 0.68 per cent. were infected with *L. loa*. Both these species of *Chrysops* were furtive in habits, lacked the voracity of other biting flies and so were seldom observed to bite man willingly—they fed mostly on cattle.

This study suggested that some other vector must transmit *L. loa*.

From two surveys of inhabitants living near breeding places of *Simulium damnosum* in areas where filarial blindness had not been observed it was found that 77 per cent. had *O. rostratus* embryos in the skin.

Antigen was prepared from avian filariae infecting wild doves and gave a positive intradermal reaction in 91 per cent. of cases (but only 4 tests are recorded, of which 2 were negative) harbouring either *L. loa* or *P. prasinus*.

P. M. ALLEN, Bahr

GIGLIOLI G. The Transmission of *Wuchereria bancrofti* by *Anopheles darlingi* in the American Tropics. *Amer. J. Trop. Med.* 1948 Jan. v 28, No. 1 71-85. [13 refs.]

Previous work is reviewed on anopheline mosquitoes of the *Anisophthalmus* group, and *Aedes aegypti* as hosts of *Wuchereria bancrofti*. The present investigations were made in two coastal areas of British Guiana where *Culex fatigans*, *Anopheles darlingi* and *Aedes aegypti* are habitual house frequenters. In one locality *Culex fatigans* predominated and in the other *Anopheles darlingi*. For the study of natural infections in wild female mosquitoes captures were made in the houses at random and the mosquitoes were brought to the laboratory and dissected the same day. Experimental infections were made with laboratory-bred mosquitoes. The technique was standardized so that early stage infections of doubtful value were excluded. More than 19,000 mosquitoes were dissected. From the evidence collected in the field and confirmed by experiment, *A. darlingi* is as good as if not better than *Culex fatigans* as vector of *W. bancrofti*. Laboratory experiments proved beyond doubt that the development of *W. bancrofti* proceeds equally well in both species.

As *C. fatigans* does not fly far from its breeding places this may account for the tendency of filarial infection to spread among the inmates of a single house. The wider flying range of *A. darlingi* presumably allows its visiting many houses thus distributing the infection over a wider area than *C. fatigans*.

Attempts to infect *Aedes aegypti* failed entirely. The experiments are fully described and the findings tabulated.

H. S. LEWIS

HARNED B. K., CUNNINGHAM R. W., HALLIDAY J. B., LEBLEY R. E., YUDA, N. N., CLARK Mary C., HINDA Carolyn H., COOPER Rachel & SUBBARAO V. Studies on the Chemotherapy of Filariasis. VI. Some Pharmacodynamic Properties of 1-Diethylcarbamyl-4-Methylpiperazine Hydrochloride, Hetrazan. *J. Lab. & Clin. Med.* 1948 Feb. 33 No. 2 16-33 8 figs. [14 refs.]

Hetrazan is a new compound which is very promising for the treatment of human filariasis (this *Bulletin* 1948 v 45 353). It has a low toxicity and few side reactions. For mice the intraperitoneal LD<sub>50</sub> (dose causing 50 per cent. mortality) was about 250 mgm. per kgm. and the oral LD<sub>50</sub> 600 mgm. per kgm.



Single intraperitoneal injections of 100 mgm per kgm were readily tolerated by mice, rats, rabbits and dogs. Rabbits tolerated daily intraperitoneal doses of 50 mgm per kgm 5 days per week for 14 weeks, rats tolerated a similar schedule of 100 mgm per kgm, and dogs treated orally tolerated 25 mgm per kgm twice daily for 2 months.

The compound was not irritating, produced no local anaesthesia, no effect upon the eye, no effect on the isolated uterus or intestine, and no effect on the blood sugar. It was mildly diuretic and analgesic. Intravenous doses of 2 to 25 mgm per kgm in unanaesthetized dogs stimulated the respiration. The heart and blood pressure were not affected by rapid intravenous injections of 0.5 mgm per kgm, but larger intravenous doses in unanaesthetized dogs produced a transient deviation from the normal. No chemical method for estimation of the drug is known at present, but experimental evidence was obtained that it is rapidly excreted by the kidney, the rate per hour in rats and mice being approximately one-third of the intraperitoneal LD<sub>50</sub>. F Hawking

WILLIAMS, R. W. Studies on the Life Cycle of *Litomosoides carinii*, Filariid Parasite of the Cotton Rat, *Sigmodon hispidus litorahs*. *J Parasitology* 1948, Feb., v 34 No 1 24-43 8 figs on 2 pls [49 refs]

ANTUNES, M. L. Notas sobre a incidência da enterobiose [The Incidence of Infestation by *Enterobius vermicularis*] *Hospital* Rio de Janeiro 1947, Dec., v 32, No 6, 971-9, 2 figs & 1 graph [12 refs]

The author examined 100 children attending his clinic in São Paulo, which is connected with the Legião Brasileira da Assistência, to determine the prevalence of infestation by *Enterobius vermicularis*. The total is, of course, far too small to give a true indication of the prevalence. He chose, as the most reliable method, the NIH swab with Cellophane. The ages of the children ranged from 2 to 10 years. Whereas only one was detected by direct faecal examination, 30 were found at the first swab examination and of 43 examined twice 12 more were detected. Thirty, or less than one in three, of the children had any itching of the anus, and 17 of these were infested and in more than half the positive cases pruritus was not a symptom. As regards age, of 23 between 2 and 3 years 6 were positive, of 31 between 3 and 5 years 14 were positive, of 30 between 5 and 7 years 15, from 7-9 years 5 out of 11, and 3 out of 5 of those up to 10 years of age. Forty-three were boys and 17 of them were positive, of 57 girls 25 were positive or 42 in all among the 100 examined. The next commonest infestation was by *Ascaris lumbricoides* (36), the third by *Trichuris trichiura* (15). *Giardia intestinalis* cysts were seen in thirty. H Harold Scott

MAC KEITH, R. & WATSON, J. M. The Diagnosis and Treatment of Threadworm Infestation. *Practitioner* 1948 Apr v 160 No 958 264-70 12 figs [13 refs]

DESCHIENS, R. & LAMY, L. La thérapie chimique de l'oxyurose [The Chemotherapy of Enterobiasis] *Liber Jubilaris J Rodhain (Soc Belge Méd Trop, Brussels)* 1947, Dec., 171-94 [13 refs]

This paper consists of a review of the literature on the chemotherapy of anthelmintic drugs, especially with reference to the treatment of *Enterobius* infection. The drugs considered include santonin, oil of chenopodium, carbon tetrachloride, tetrachlorethylene, bismuth carbonate and subnitrate, the derivatives of triphenylmethane—*e.g.* alkaline fuchsin, gentian violet and

Nutritional neuropathies are considered in four groups —

1. Peripheral neuritis, including "electric feet" and cranial nerve lesions.
2. Nutritional amblyopia.
3. Spinal cord involvement.
4. Mental changes.

These manifestations are regarded as parts of a single syndrome based aetiologicaly upon a prolonged protein deficiency with a high relative carbohydrate intake and multiple vitamin deficiencies of the B group.

Factors which may be responsible for the distribution of the lesions in the central nervous system are considered in detail and the author concludes that the most important of these factors is phylogenetic seniority the younger tracts being selected first the sensory mechanism being relatively more sensitive than its motor counterpart.

Dean I. Smith

HERNÁNDEZ CÁRERO A. Beri-beri cardíaco. (Caso clínico) [A Case of Cardiac Beri-beri.] *Salud y Beneficencia Social* vol. 11, no. 4, 1947, p. 117. Oct.-Nov. Dec. 7 No. 4 11 1947 figs.

GILMAN J & GILMAN T. Liver Disease in Johannesburg: relation to Pellagra. *Lancet*, 1948, Jan. 31 169-73. (16 refs.)

In an earlier paper [this *Bulletin* 1946, v 43 364] the authors have described the pathological findings in biopsy specimens of the liver from Africans with pellagra. The changes were classified under four headings, and further subdivided according to the amount of fat present. The types were —

- i. Fatty infiltration alone.
- ii. Cytosclerosis or accumulation of an iron-containing pigment in hepatic and Kupffer cells.
- iii. Cytosclerosis, as in type ii, but with large masses of iron pigment in Kupffer cells and histiocytes of the portal tracts.
- iv. Pigment cirrhosis.

The present paper provides a background for these observations. A survey has been made of the histology of the liver in a sample of the general population, represented by an unselected series of 351 people killed by trauma. The same

	General population		Pellagrics
	Africans	European	
Number of cases	281	80	17
Percentage incidence of lesions			
Type i	7	13.3	4.9
" ii	43.7	36.6	35.7
" iii	28.4	11	23.7
" iv	9.6		9.7
Normal	12.6	4	—
Other lesions	3.0	4.6	—

classification has been used, and the results of the two investigations may be most conveniently compared in a table, derived from two tables in the authors' text

These figures show a remarkable correspondence between the pellagrins and the general population of Africans in the incidence of all except the type 1 lesions. The more chronic changes (types iii and iv) were much less common in Europeans than in Africans. There are two further significant points not brought out by this condensed table: the changes in general were less severe in Europeans than in Africans. Even slight degrees of fatty infiltration or cytosiderosis have been included in the table as type 1 or type 11 lesions. Whether these slight changes should be regarded as pathological is a point upon which the authors do not commit themselves. Secondly, the lesions of all types occurred earlier—by one or two decades—in pellagrins than in the general population of Africans, and earlier in Africans than in Europeans.

The authors have extended their original conception of the way in which these pathological changes are related. "Cirrhosis can supervene at any stage in the course of cytosiderosis, and not only when the liver becomes intensely pigmented." They re-emphasize that cirrhosis is not related to long-standing fatty change. Siderosis, or the appearance of masses of pigment in Kupffer cells and histiocytes, may also develop at any stage in the evolution of cytosiderosis. "Both reactions—namely, cirrhosis and siderosis—represent distinct landmarks in the progress of the disease."

The consequences may extend beyond the liver. It is suggested that the discharge into the circulation of inert pigment of large molecular size may have important effects on other organs, analogous to those produced experimentally by the injection of synthetic polymers, and described by HUEPER (*Arch Pathology*, 1942, v 33, 267) under the name 'macromolecular syndrome'.

Since liver lesions are as common in the general population of Africans as in pellagrins, the question arises of the relationship between pellagra and cytosiderosis. The fact that pigment changes are more extensive and severe in pellagrins suggests that a relation does exist, but this cannot yet be defined with precision. The authors' view may be given in their own words: "In the general population of Africans some types of stimuli are maintaining a perverse intracellular metabolism, having as an end-result the deposition of iron pigment."

This perverse metabolism can silently destroy the tissues to such an extent that the patient first becomes severely ill and presents himself at the hospital when he already has an advanced hepatic cytosiderosis with or without cirrhosis.

At any stage during the progress of this pathological process, which to the untrained observer does not express itself clinically as an acute attack of pellagra may be suddenly precipitated."

J C Waterlow

DAVIES, J N P. The Essential Pathology of Kwashiorkor. *Lancet* 1948, Feb 28, 317-20 [25 refs.]

The term kwashiorkor has in recent years been extended by Trowell to include adult as well as infantile cases. Some patients may present in a chronic phase of the disease, with few specific signs except for the presence of undigested food in the stools. This paper describes the histological findings in 50 cases examined at post-mortem or by biopsy, 31 of the patients were less than 10 years old.

In the liver, the histological picture varied with the age. In children under 5 there was always some degree of fatty change. This began in the cells in the peripheral parts of the lobules, and progressed towards the centre, until

eventually every liver cell was loaded with fat. The appearance of fat was accompanied by infiltration of lymphocytes into the portal areas, and proliferation of reticulin fibres into the lobules, surrounding and strangling the peripheral cells. If resolution occurred the fat disappeared first from the centro-lobular regions and last from the periphery. Great stress is laid on the predominantly peripheral distribution of the fat—if fat is mid-zonal, central or irregular—some serious complication is to be suspected, and the condition is probably secondary kwashiorkor. The disappearance of fat may or may not be accompanied by clinical improvement. When all fat has disappeared, the liver is left with a patchy monolobular cirrhosis, with collections of lymphocytes at the edges of the lobules. This picture is the "hallmark of kwashiorkor" and persists throughout life. It has been found in almost every case in a series of more than 1,000 post mortems.

In older children and adults, fatty change was absent or slight except in a group of adult immigrants from the Belgian Congo. All cases presented the typical clinical picture of kwashiorkor regardless of whether the liver was fatty. Therefore the fatty change so prominent in infants, cannot be looked upon as the essential lesion in this disease. With increasing age the fibrosis became more severe—the final picture was a pure monolobular cirrhosis similar to that described by VINT (this *Bulletin* 1931 v. 23, 844). In most cases this seemed to be complicated in the later stages by focal necroses with regenerative hyperplasia and replacement fibrosis producing a mixed type of cirrhosis. In contrast to the findings in Johannesburg there was no excess of iron pigment and the condition never progressed to haemochromatosis. Malaria and helminthiasis were present in a few cases, but there was no evidence that these were related to the liver lesions.

Changes were also found in the kidney and pancreas. The kidneys showed hyalinization of the glomeruli, with metaplasia of the capsular epithelium and pericapsular fibrosis.

In the pancreas the earliest change was atrophy of the acinar cells, followed by hyalinization and fibrosis. In late cases the acini had disappeared over wide areas of the pancreas. Cyst formation and metaplasia of the ductal epithelium were not found—the condition therefore differs from cystic fibrosis of the pancreas described by AXENBERG (*Imperial J. Dis. Children* 1938 v. 36, 344). There was an indication that in the early stages the islets were hyperplastic later some seemed to disappear.

Attention was first directed to the pancreas because some patients admitted as diabetics in hyperglycaemic coma, when treated with insulin passed into hypoglycaemic coma which did not respond to treatment with glucose. At post-mortem the pancreas in such cases was found to be almost completely fibrosed. It was then discovered that fibrosis of the pancreas was extremely common. It was found in two-thirds of 163 routine autopsies and in every one of 13 cases of kwashiorkor. It is therefore suggested that pancreatic fibrosis is a kwashiorkor lesion, and that the disease is initially a result of pancreatic deficiency itself caused by malnutrition. This view is supported by the constant finding of undigested and unabsorbed food in the stools. It could also explain the common but not invariable association of kwashiorkor with fatty infiltration of the liver—since fatty liver has been produced in dogs by extirpation of the pancreas.

If this assumption is correct treatment should logically be directed to restoring pancreatic function. In this connexion the interesting observation has been made that one of the first signs of clinical improvement was swelling of the salivary glands which are closely related morphologically to the pancreas.

J. C. WATSON

MAGALHÃES CARVALHO, PINTO, A. G., SCHMIDT, M. M., POTSCH, N. & COSTA, N. Distrofia pluricarenal hidropigênica [Dystrophy with Oedema and Signs of Multiple Nutritional Deficiency] *J. Pediatría* Rio de Janeiro 1945, Nov-Dec, v 11, Nos 11/12, 395-439, 7 graphs & 7 figs [83 refs]

— A esteatose hepática na distrofia pluricarenal hidropigênica da infância [Fatty Liver in Infants with Dystrophy, Oedema and Multiple Nutritional Deficiency] *Medicina, Cirurg, Farmacia* 1946, June, No 122, 1-16 [17 refs]

DE MAGALHÃES CARVALHO, J. Contribuição ao tratamento da distrofia pluricarenal hidropigênica [A Contribution to the Treatment of Dystrophy with Oedema and Multiple Nutritional Deficiency] *Hospital* Rio de Janeiro 1947, Sept, v 32, No 3, 307-26, 6 figs [28 refs]

Oedema was the criterion used in selecting the cases described in these three papers. The syndrome as a whole, however, appears to be identical with kwashiorkor in Africa [The word is here used in its original sense (see WILLIAMS, *this Bulletin*, 1934, v 31, 344) and not with the wider meaning recently attached to it by TROWELL (*ibid*, 1945 v 42, 306)]. The age incidence ranged from 4 months to nearly 6 years. Of 58 cases, 14 were white, 32 mixed, and 12 black. [The racial incidence is of interest because kwashiorkor has seldom been described in white children. It has been suggested that the disease is confined to peoples of African stock—a theory that can no longer be upheld in view of the present results from Brazil the observations of HANAFY (*this Bulletin*, 1948 v 45 458) in Egypt and earlier reports from Central America.]

The history was of a diet consisting almost entirely of carbohydrate. Diarrhoea was common. In many cases the presenting sign was oedema. This was of the dependent type, sometimes generalized and very severe. The skin was dry and inelastic, with branny desquamation. In most cases there was an extensive, diffuse hyperpigmentation, described as "Addisonian". Thirty-eight cases showed other skin lesions as well, most commonly there were irregular hyperpigmented patches with sharply defined edges and a more or less symmetrical distribution. The sites of election were the thighs, perineum, and gluteal region. The lesions began as discrete papules round hair-follicles, these became pigmented and coalesced, the pigmentation deepened, and the superficial layers desquamated leaving a delicate pink skin underneath. Biopsy of the skin showed atrophy of the basal and Malpighian layers with oedema and degenerative changes in the corium. These findings are illustrated in the first paper by photomicrographs. The lesions were more common in the black children than in the white or mixed. In other cases there were smaller hyperpigmented areas which appeared without initial erythema.

The hair was, in general, dry and depigmented, and the scalp covered with seborrhoeic crusts. In a few cases there was xerophthalmia. Angular stomatitis was common. The tongue usually showed atrophy of the papillae, although in some cases there was a frank glossitis. Examination of the heart showed tachycardia with marked sinus arrhythmia. Occasionally inversion of the T-wave was found in more than half the cases, and the calves were tender to pressure. The liver was usually enlarged, with a smooth regular edge, but the spleen was not palpable. At post-mortem, gross fatty infiltration of the liver was a constant finding. This was not related to the degree of enlargement. Other autopsy findings are not recorded. Evidence of osteoporosis was observed in X-ray examinations. Laboratory examinations were mainly of negative interest. Helminthiasis was found in only a quarter of the cases. There was a variable degree of anaemia sometimes with a mild macrocytosis. Estimations on serum showed

in the mean values for calcium (7.39 mgm. per cent.) phosphorus (3.36 mgm. per cent.) cholesterol (88.5 mgm. per cent.) and phospholipids (8.1 mgm. per cent.). The total protein and albumin concentrations were very low but the globulin content was normal (means 4.13, 1.97 and 2.17 gm. per cent. respectively). The relation of these findings to oedema is discussed at length in the first paper. Although in most cases total protein and albumin concentrations were below the so-called oedema level this was not always so. Moreover in cases responding to treatment it was sometimes found that, as oedema disappeared the total protein and albumin concentrations did not rise but were even further reduced. It is suggested that the serum proteins may be not only reduced in quantity but also qualitatively altered in such a way that they do not exert their normal osmotic pressure and that under treatment the normal composition is restored before the amount.

Analysis of these findings showed that the condition was one of multiple deficiency involving protein minerals, vitamin A, thiamin riboflavin, nicotinic acid and probably other members of the vitamin B<sub>2</sub> complex. However at an early stage it was found that, in spite of the presence of signs of specific deficiency treatment with the vitamins concerned not only failed to cure but actually made the disease worse. Moreover none of the signs noted seemed to be in any way related to the severity of the general condition or to be of any value in assessing the prognosis. For these two reasons from the end of 1944 onwards attention was focussed on the fatty liver which was felt to be the central feature of the disease.

The harmful effect of vitamins was explained by the experimental findings of HANDLER, McHENRY and others that in rats choline-deficiency does not produce a fatty liver if B-vitamins are absent from the diet. Under the conditions of their experiments, when vitamins were given, the amount of fat in the liver increased. Moreover since diets low in the B-complex are likely also to be low in choline, it was logical to suppose that the fatty liver in these infants was the result of choline deficiency. This theory was tested by giving choline in various doses, and measuring the serum phospholipid content after an interval of 8-48 hours. It was thought that on current theories of the lipotropic action of choline, there should be an increase. No such increase was found, nor did there seem to be any beneficial effect on the general condition.

On the theory of choline-deficiency it was difficult to explain the presence of fatty liver in these infants in spite of an inadequate intake of B-vitamins as shown by the clinical signs of avitaminosis. Magalhães Carvalho and his colleagues therefore turned their attention to types of fatty liver that are not caused by choline-deficiency such as that produced in dogs by excision of the pancreas and cured by the pancreatic extract lipocac. Fifteen cases were treated with lipocac with apparent success. The authors are however careful to point out that the results were not significantly better than with milk alone and that the main point in treatment is to avoid giving vitamins. The results in detail were as follows —

Dried skimmed milk with vitamins, liver extract and plasma, etc.	35 cases, 10 deaths
Dried skimmed milk alone	8 cases, 1 death
Dried skimmed milk with lipocac	15 cases, no deaths

The rôle of the pancreas was further emphasized by the finding that in our latest cases there was a reduced secretion of pancreatic lipase and trypsin. These observations are briefly mentioned and not reported in full. The conclusion is drawn that in this syndrome the primary and essential lesion may be of the pancreas and not of the liver.

## Comment

[The discovery of anatomical and functional lesions of the pancreas in kwashiorkor marks a new and important stage in our knowledge of the disease. It is remarkable that the same conclusion should have been reached independently and more or less simultaneously in three different parts of the world. In addition to the work of DAVIES and of MAGALHÃES CARVALHO, Professor VÉGHÉLYI has recently (*Lancet*, 1948, Mar 27, 497) reported from Budapest that when infants were deprived of milk during the siege, there was a decrease of pancreatic secretion which preceded the development of nutritional oedema and fatty liver. Such observations form a logical sequel to the earlier work of Scott BROWN and TROWELL [this *Bulletin*, 1945, v 42, 306] on the deficiency bowel pattern.]

Atrophic changes in the pancreatic acinar cells were observed in infants with fatty liver in the West Indies [WATERLOW, this *Bulletin*, 1947, v 44, 841] but no conclusions were drawn about the relationship between the two lesions. Magalhães Carvalho implies, and Davies explicitly suggests, that fatty liver may be secondary to pancreatic damage, on the analogy of the fatty liver produced in dogs by pancreatectomy. This fits in with the fact that the disease does not respond to treatment with methionine [GILLMAN and GILLMAN, *ibid*, 1945, v 42, 748] or choline [MAGALHÃES CARVALHO, above, WATERLOW, *ibid*, 1947, v 44, 841, *Med Res Council Spec Rep Ser No 263*, 1948], whereas most workers have obtained good results with milk alone (Véghelyi, Magalhães Carvalho, Waterlow). The final link in the chain may be provided by the observations of FRIEDMANN and FRIEDMANN (*Canadian Med Ass J*, 1946, v 55, 15) who produced atrophic changes in the pancreas and fatty liver in rats on a diet low in protein.

If, as Davies suggests, kwashiorkor is essentially a pancreatic disorder, it would resolve a puzzling paradox. TROWELL [this *Bulletin*, 1941, v 38, 722, 1945, v 42, 306] has convincingly described the disease as a multiple deficiency state, involving almost all known factors. For this reason its limits have been extremely hard to define. At the same time, all observers have clearly felt that it is a definite disease, and this feeling has inspired a constant search for an essential lesion. The apparent contradiction would be removed if the essential lesion were one involving the splitting, absorption, and intestinal synthesis of nutrients.

It has become increasingly clear from the careful work over many years of Trowell, the Gillmans, and their collaborators, that kwashiorkor cannot be looked upon as an isolated episode of infancy or early childhood. Its consequences extend throughout life, since it may cause irreversible changes such as fibrosis of the pancreas and liver, and other lesions of which we know little. Moreover, even in adult life, the causes of kwashiorkor are never far away. The diet remains insufficient and unbalanced, so that the resulting picture is often very complex—of acute episodes superimposed, in the Gillmans' phraseology, on the chronic effects of a perverted metabolism.

Thus, even if it is established that the initial lesion is in the pancreas, there is much that remains to be discovered about the natural history of the disease and the relationship of its various features. In particular, great interest attaches at the present time to the pathological changes found in the liver, both in children and adults. It may therefore be of interest to examine in greater detail some of the observations in the papers summarized above.

In their earlier work Gillman and Gillman implied the existence of a close relationship between cytosiderosis of the liver and pellagra. This position led to difficulties. In the first place, cytosiderosis does not appear to have been found in pellagrins elsewhere, secondly, it tended to narrow the field of enquiry.

into the cause of the liver lesion. It is clear however from their present paper and that of Davies that liver lesions in Africans are almost universal: their distribution in fact is wider than that of pellagra, malignant malnutrition, or kwashiorkor in its infantile form (this *Bulletin* 1934 v. 31 344). Cytosiderosis cannot be regarded as a hallmark of pellagra, since it is equally common in non-pellagrins. It may therefore seem illogical to look upon monolobular fibrosis as the hallmark of kwashiorkor. This difficulty is avoided by the statement of Trowell that every African passes through a kwashiorkor phase manifested by pot belly and failure of growth. The connexion between this malnutritional phase and the ever present fibrosis cannot however be regarded as proven. This caution is dictated by the fact that whereas cirrhosis is admittedly common in malnourished peoples, this particular type of monolobular fibrosis seems not to have been described outside Africa.

In the case of fatty liver Davies has shown that this cannot be a kwashiorkor lesion since cases may present all the clinical signs of that disease with no fat in the liver. The complement of this has been found in the West Indies (WATKINSON *loc. cit.*). Infants may show gross fatty infiltration of the liver and die apparently from hepatic failure with oedema but none of the other manifestations of kwashiorkor. There was also evidence obtained by biopsy that milder degrees of fatty change were quite common in infants apparently healthy except for slight weight loss. Therefore it would seem that in babies fatty liver may be looked upon as a distinct entity, an effect of malnutrition separable from other signs of deficiency. It is in no way specific to kwashiorkor but may also be found in malnourished infants in Europe as in cases of *malnutrition* (WATKINSON 1947 v. 42 424).

The conclusion then must be that liver lesions of various types (fatty change, cytosiderosis, cirrhosis) are widespread among the malnourished populations of the tropics but it is not yet possible to relate any particular lesion to a specific clinical picture.

When the papers of Davies and the Gillmans are considered together the question arises why should iron pigmentation be found in one group and not in the other? An answer is yet possible. Cytosiderosis, as far as present information goes, seems to be peculiar to the Rand whereas cirrhosis in one form or another is common throughout the tropics. An important observation which may be relevant has been made by GILLMAN and GILLMAN (1945). In refuting the view that cytosiderosis might be caused by anaemia, they pointed out that their patients were not anaemic, and did not suffer from malaria or ankylostomiasis. All these conditions are endemic in East Africa, and in most parts of the tropics. It is therefore possible that other things being equal the absence of cytosiderosis is related to the presence of diseases which increase the body's demand for and turnover of iron.

The end-results of fibrosis in the liver tend to be much the same whatever the initial cause. Therefore conclusions derived from experimental cirrhosis in animals cannot easily be applied to man until more is known about the development and early stages of the human disease. Davies's observation are here particularly valuable and go far to fill the gap although none of the types of dietary cirrhosis produced in animals corresponds exactly to monolobular cirrhosis in man. It is not clear whether the workers in East Africa believe that fibrosis is in any way caused by fatty infiltration. In the West Indies the same picture was found, of a tumour mass growing into the edge of the liver lobule (WATKINSON *loc. cit.*). From the scanty evidence available it seemed that the end result was a fibrosis of the Laennec type similar to that produced in dogs with fatty liver by CHAIKOFF and his co-workers (*Am. J. Path.* 1943 49 9).

This brief summary draws attention to three questions in relation to the liver lesions —



- 1 Is fibrosis caused by preceding fatty infiltration ?
- 2 Is fibrosis of the liver, as found in under-nourished peoples, a pathological entity, or does it have different modes of development under different circumstances in different parts of the world ?
- 3 What is the relationship of iron pigmentation to the other changes ?

It is clear that these questions can only be fully answered in the light of information from all parts of the world where malnutrition exists. In recent years the study of the more acute forms of the disease has gone forward with great speed in many different countries, and this gives great promise for the future.]

J C Waterlow

## HAEMATOLOGY

GOSDEN, Minnie & REID, J D **An Account of Blood Count Results in Sierra Leone** *Trans Roy Soc Trop Med & Hyg* 1948, Mar, v 41, No 5, 637-40

This paper analyses the results of 1,035 total red cell and 1,005 white cell counts done on adult Africans at the Government Laboratory, Freetown, between 1943-1946

The chief object of the survey was to compare adult African blood standards with European "normals" and to determine the locally prevailing types of anaemia. The samples were those for routine examinations for anaemia or from patients who felt "run-down". The patients came from all social grades, but classification on a social basis was not possible in view of varying dietetic standards, such a classification would have been a factor of importance.

Many of the anaemias did not respond to either iron or liver therapy alone, and required a combination of both. They probably corresponded with Trowell's dimorphic type [this *Bulletin*, 1943, v 40, 938]

Standard methods of examination were employed and are described and the European standards adopted for comparison were those given by WHITBY and BRITTON (*Disorders of the Blood*, 1942, 4th Edition London Churchill)

The results are shown in four tables. These show that 26 per cent of 661 men had red cell counts of at least 5 million cells per cmm and 72 per cent were at least 4 million. About two-thirds of the latter had normal values for mean corpuscular haemoglobin and mean corpuscular volume. Of 377 women, 56 per cent had red cell counts of at least 4 million cells per cmm, and of these over half had normal MCH and MCV values.

In 109 moderate anaemias in men 57 per cent were orthochromic normocytic and of the 74 more severe anaemias 40 per cent were orthochromic and 39 per cent were normocytic. Hypochromic microcytic anaemia was about twice as common as macrocytic hyperchromic anaemia.

In 99 moderate anaemias in women, about half were orthochromic normocytic and this form was also seen in 64 severe anaemias. The microcytic hypochromic type was about 3 times as common as the macrocytic hyperchromic type.

The sickle cell trait was found in 27 per cent of all the bloods examined.

Of the white cell counts in 646 men and 359 women, 79 per cent were within normal limits and 5 per cent showed leucopenia, eosinophilia occurred in 40 per cent of men and 17 per cent of women and a monocytic increase was present in 34 per cent of men and 42 per cent of women.

During the same period, 7 cases of myeloid and 1 of lymphatic leukaemia were seen.

The authors conclude that in adult Africans in the Freetown area blood cell counts and haemoglobin levels appear to be within the accepted normal levels.

for Europeans that an orthochromic normocytic anaemia is the commonest type that microcytic hypochromic is commoner than macrocytic hyperchromic and that about one adult in four has the sickle-cell trait.

[It is now almost a platitude to observe that efforts to arrive at haematological and other "normals" in Africans are of prime importance and until acceptable physiological standards are arrived at many forms of pathological research must remain without an adequate foundation. Surveys of the kind described above are greatly to be commended but the difficulty still remains of assessing the normal "African" in the first instance for example in the above series all the persons examined were patients complaining of some degree of ill-health. The present reviewer in a small study of the polymuclear count in East Africans many years ago (this *Bulletin* 1931 v 28 837) set out to obtain a control series of healthy Africans who would be sufficiently free of any disease—and particularly any infection—which might be likely to influence their haematological state. Experience showed what immense difficulties existed anything which clarifies the physiology of Africans in their present background increases the possibilities of understanding and therefore rectifying their pathological status. See also HENNESSY this *Bulletin* 1937 v 34 36.]

H J O'D Burke-Gaffney

BOTURLO Edg & BOTURLO Edm. Duença por hemalias folciformes (Sickle-Cell Disease). Incidência na Santa Casa de Santos—observações clínicas e haematológicas. [Observations on Cases of Sickle-cell Anemia in Santa Casa Hospital (Rio de Janeiro).] *Hospital*. Rio de Janeiro 1947 Nov v 32, N 5 709-28, 4 figs. (38 refs.) English summary

Three cases of this condition are described from among 20 detected in examining 294 coloured persons. 64 white persons were examined, but none of these was affected. Of the 294 there were 162 negroes and 132 mulattoes and those with sickle-cell numbered 14 and 6 respectively. The histories of the three were very different. One (No. 3 in the cases detailed) had fever, cough, and pain in the chest and was diagnosed as suffering from lobar pneumonia. A second (No. 2) had fever, palpitation, dyspnoea, tinnitus and prostration from weakness. The third (No. 1) in the midst of enjoying excellent health suddenly complained of "feeling very ill" and lost consciousness. He was brought to hospital in a comatose condition which persisted for 7 days and was followed by transient aphasia and dysarthria, so that no proper account could be obtained for 10 days and even then there was some degree of mental confusion but he remembered telling his fellow worker that he was feeling ill. Wassermann reaction was negative with both serum and cisternal fluid. The blood changes are described fully and were those usually seen in this disease: the sedimentation rate was much reduced ranging between 3 and 15 mm. in the first hour. The erythrocyte count also varied widely. In No. 1 it was 3,480,000 and Hb 80 per cent. and 7 weeks later 4,400,000 with Hb 85 per cent. In No. 2, the first count gave only 800,000 per cmm and Hb 30 per cent. 3 weeks later 2,000,000 and Hb 62 per cent. after another week he had another febrile attack and the red cells fell to 650,000 and Hb to 18 per cent., increasing in a fortnight to 1,740,000 and Hb 45 per cent. After this he improved slowly but at times complained of headache and giddiness and had occasionally bouts of fever to 40°C. No. 3 was not so ill: his counts ranged during the first ten days observation about 2-4 million per cmm and Hb 40-50 per cent. and in another ten days the figures were 3,120,000 and 60 per cent. The residual red corpuscles in 0.2 per cent. saline in this patient became elliptical and remained so for 24 hours. These are regarded by the author as "regression forms" of the sickle erythrocytes possessing greater resistance.

H Harold Scott

FARRER, VALENTI, P. 'Laquímica y fisiología de las anemias carenciales' (Conclusión de las lecciones y ponencia presentada) (Physiopathological and Clinical Aspects of Nutritional Anaemias, other than Iron Deficiencies and Pernicious Anaemia.) *Semin. Med.* 1945, 11, 1, 55. No. 10, 283-291, 1 fig. (37 refs.)

## VENOMS AND ANTIVENOMS

MACCHIARELLO, A. Cutaneous Arachnoidism experimentally produced with the Glandular Polson of *L. xiphioides*. *Puerto Rico J. Pub. Health & Trop. Med.* 1947, Dec., v. 21, No. 2, 260-79. 4 figs. Spanish version 281-93.]

Study has been undertaken of the poison or poisons of the spider *L. xiphioides* which occurs in Antioquia, Chile. The lesion produced in man is known as 'gugigerous spot'. The spider abounds in damp, dark and dry places, and many were captured in mud and straw hut. Experiments were made with rabbits, rats and white mice at first, but later guinea pigs were used solely. The lesion is a severe, generalized oedema without induration to oedema with induration and to a urticarial spot followed by necrosis and ulceration. In man the same sequence of events occurs, but without general systemic disturbance. The severity differs from one patient to another, and whether the bite (or sting) is the first or not, and whether the insect has been kept caged and fasting. Stings of the black or greenish black specimens are the worst, they are usually the young ones. The more concentrated the poison (that is glandular matter ground up and emulsified in saline) the less intense the reaction: this is ascribed to the fact that the concentrated poison causes coagulation of the tissues and thus impedes diffusion. The glandular poison seems to act only on or in the skin: it is not haemolytic. The arachnism extracted from the cephalothorax or abdomen differs in its action from the glandular poison from the fangs and there is no cross-immunity between them. Moreover, the arachnism is strongly haemolytic for guinea pig erythrocytes and still more for rabbit corpuscles and is not necrotizing.

H. Harold Scott

RAMIREZ L. R. Obtencion de veneno de alacran por estimulación eléctrica. (The Extraction of Venom from Scorpions by Electrical Stimulation.) In *Escuela Vac. Ciencias Biol.* Mexico 1947, Aug. 15, v. 1, No. 4, 383-5. 1 figs. English summary (5 lines.)

RAMIREZ L. R. Datos preliminares físicos y químicos del veneno de alacran. (Preliminary Data on the Physical and Chemical Characters of Scorpion Poisoning.) *An. Escuela Vac. Ciencias Biol.* Mexico 1947, Aug. 15, v. 1, No. 4, 379-82. [11 refs.] English summary

## DERMATOLOGY AND FUNGUS DISEASES

LEÓN BLANCO, F. & DE LAOSA, O. The Primary Lesion of Pinta (Mal del Pinto or Carato). *Amer. J. Syph.* 1947, Nov., v. 31, No. 6, 600-609, 9 figs.

There are three stages in the clinical course of pinta, the initial lesion, secondary widespread skin lesions or pintides and the tertiary dyschromic stage. The present study was presumably carried out in Cuba.

Five to ten days or earlier after infection a small papule develops. By the 20th to 26th day it is larger flat and slightly desquamating. By the 30th-50th day the lesion is a flat reddened scaly patch. Satellite papules may develop and later coalesce with the enlarging initial lesion. The final appearance may resemble psoriasis, trichophytosis, lichen or may be that of large pink desquamating patches with infiltrated edges which are often separated by atrophic skin.

In the early papular stage, itching is constant but it is less marked later. The initial lesion is usually on an exposed part of the body especially the leg and dorsum of the foot (63 per cent of 257 cases) and the forearm and dorsum of the hand (22 per cent.).

The disease is usually acquired during the first two decades of life but begins after the first year or so.

The lymphatic glands, in the primary and secondary stages are enlarged, painless and movable.

The incubation period in experimental infections is 3-10 days, but longer periods up to 60 days, have been reported.

In 39 naturally acquired infections of 40 days to two years duration, the serologic flocculation and complement fixation tests were negative. In 17 experimental infections the reactions became positive after the appearance of pustules.

The histopathological changes in the initial lesion include acanthosis with increased length of narrow rete processes, active infiltration by lymphocytes and polymorphonuclear cells and the development of oedema. In the cutis there is peri-vascular infiltration by lymphocytes and plasma cells. *Tropone-mata* are numerous, particularly in the epidermis. [The illustrations of initial lesions are excellent.] See also this Bulletin 1945, v 42, 584.]

C J Hackett

ALLEN A. C. Persistent "Insect Bites" (Dermal Eosinophilic Granulomas) simulating Lymphoblastomas, Histiocytoses, and Squamous Cell Carcinomas. *Amer J Path.* 1948, Mar v 4 No. 3 357-87 24 figs. on 8 pls. [11 refs.]

This article describes the histology of the cutaneous reactions to "bites" of ticks, chiggers, mosquitoes and unidentified arthropods. The author emphasizes that these reactions may last as long as two years and may exhibit a very variable microscopical picture. The cellular reaction in the dermis, characterized by large numbers of eosinophilic leucocytes, plasma cells and histiocytes, may be mistaken for Hodgkin's disease, mycosis fungoides, atypical lymphoblastoma, histiocytoses or the eosinophilic granular group. An appearance closely simulating that of squamous-cell epithelioma may be produced by a section which cuts obliquely through the hyperblastic epidermis and its branching rete pegs. No difference was noted in the histological reaction to bites of the various arthropods except for the almost complete absence of eosinophilic leucocytes in the eschar of scrub typhus caused by the larval mite (*Trombicula akamushi* and related species).

H F H B A

JOLLY H. R. Prevention of Ringworm in the Tropics. *Brit Med J* 1948, Apr 17 738-8, 1 graph

This article describes an experiment in the control of ringworm in the Netherlands East Indies where the disease had reached epidemic proportions and very severe cases were not uncommon. Four hundred British troops were selected for the experiment, which aimed at the prevention of spread of infection from the feet of one soldier to those of another.

Two pairs of underpants were issued to each man, and these were washed and changed daily. Each man was given two foot-towels, which were used on the feet only, and were washed and changed daily. Clogs were provided to be worn in the bathroom, where showers were used and not baths. This enabled the toes to be washed without removal of the clogs, and consequently the feet were never brought into contact with the bathroom floor. The men were not allowed to walk bare-footed around the buildings.

Infected cases were not segregated, and the following routine treatment was used with occasional modifications —

Lesions on the body — One per cent chrysarobin in Lassar's paste

Lesions on the face — Whitfield's ointment

Lesions between the toes — Brilliant green 1 in 500 in spirit with 3 per cent salicylic acid

By these means, the number of new cases of ringworm was reduced from 91 in May 1946 to 13 three months later, and this result was achieved without interference with the normal working routine

H T H Wilson

HOWELL, A, Jr. The Efficiency of Methods for the Isolation of *Histoplasma capsulatum*. *Pub Health Rep* Wash 1948, Feb 6, v 63, No 6, 173-8, 3 figs on 2 pls [11 refs]

From the spleens of 79 guineapigs experimentally infected with a single strain of *Histoplasma capsulatum*, sowings were made in duplicate on two different culture media, brain-heart-blood-agar and potato-dextrose-agar with penicillin and streptomycin added. One set of cultures was incubated at 37°C and the other at room temperature.

Of the cultures incubated at room temperature, 35 out of 46 (76.1 per cent) on brain-heart-blood-agar and 19 out of 46 (41.3 per cent) on potato-dextrose-agar were successful, while those incubated at 37°C yielded only 6 successful growths out of 46 sowings on brain-heart-blood-agar and none on potato-dextrose-agar. These results would indicate that brain-heart-blood-agar is a more suitable medium than potato-dextrose-agar and incubation at room temperature much better than at 37°C. [It should be noticed, however, that only a single strain of *H. capsulatum* was used, and strains of this species vary in their adaptability to saprophytic vegetation at 37°C.] [Only the mycelial form of the fungus is mentioned in the paper and it is well known that the optimal temperature for vegetation in this form is far below 37°C in fact some strains cannot vegetate in the mycelial form at this temperature. On the other hand, 37°C is the optimal temperature for vegetation in the yeast-like form and, on blood-agar at this temperature yeast-like primary cultures frequently develop. Subject to this qualification, the author's findings are in harmony with the general experience of mycologists.]

J T Duncan

CROSS, F W & HOWELL, A, Jr. Studies of Fungus Antigens II Preliminary Report on the Isolation of an Immunologically Active Polysaccharide from Histoplasmin. *Pub Health Rep* Wash 1948, Feb 6, v 63, No 6, 179-83

The polysaccharide fraction was isolated from crude histoplasmin by precipitation with ethyl alcohol (4 vols of 95 per cent) after previous removal of the protein fractions. The yield of dry polysaccharide was approximately 0.34 mgm per ml of the crude solution. Tests of dermal sensitivity made on a group of guineapigs experimentally infected with *Histoplasma capsulatum*, and a number of normal control animals showed the polysaccharide to be an effective reagent. Compared with the stock, crude histoplasmin, and desiccated

crude material, the polysaccharide at a dose of 0.1 mgm. in 0.1 ml. gave a positive reaction in 83.9 per cent. of the guinea-pigs sensitized with *H. capsulatum* histoplasmin at a dose of 0.1 ml. of 1:100 solution, in 85.3 per cent. and desiccated histoplasmin at a dose of 0.1 mgm. in 0.1 ml. in 81.6 per cent. Lower proportions of reactors and smaller reactions were given by all three reagents when they were used in lower dosage but even at the dose of 0.001 mgm. per ml. the polysaccharide gave positive results in 45.5 per cent. of the animals.

As the polysaccharide fraction represents only about 1 per cent. of the total solids of histoplasmin, it seems that there are other antigenic fractions in the crude material.

To test for cross reactions guinea-pigs infected with *Blastomyces dermatitidis* which were highly sensitive to blastomycin, were used with the histoplasma polysaccharide. The proportions of positive reactors at the various doses were as follows: 0.1 mgm. 48.1 per cent., 0.01 mgm. 25.9 per cent. and 0.001 mgm. 3.7 per cent. The comparable proportions with *Histoplasma* inoculated animals were 83.9 per cent., 78.8 per cent. and 45.5 per cent.

J. T. Duncan

TENENBERG D. J., HOWELL, A. Jr., FURCROW M. L., BUXNELL, L. L. A Complement Fixation Test for Histoplasmosis. I. Technic and Preliminary Results on Animal Sera [TENENBERG & HOWELL] *Pub. Health Rep. Wash.* 1948 Feb. 6 63 No. 6 163-8. II. Preliminary Results with Human Sera [FURCROW, BUXNELL & TENENBERG] *Ibid.* 169-73.

The significance of dermal sensitivity to histoplasmin in the absence of clinical and mycological evidence of active histoplasmosis remains undetermined. It is imperative therefore that the diagnostic value of serological tests in this disease should be explored.

I. The first paper deals with the complement fixation test applied to the serum of experimentally infected guinea-pigs. The antigen used was the 1:100 dilution of the histoplasmin skin test reagent (H.15) and the technique was based on Kolmer's modification of the Wassermann test. Of the sera from infected guinea-pigs 5 out of 1 gave complete fixation of complement while sera from 33 uninfected guinea-pigs all gave negative results. Cross reactions between *Histoplasma* antiserum and *Blastomyces* antigen (the 1:100 blastomycin skin test reagent) and between *Blastomyces* antiserum and *Histoplasma* antigen occurred but by preparing serial dilutions of the serum a point could be reached at which complement fixation was given only with the homologous antigen. These cross reactions when relatively low dilutions of the sera are used are in harmony with the cross reactions described by HOWELL *Bull. of Hyg.* 1947 v. 22, 569 in connexion with the histoplasmin and blastomycin skin sensitivity tests. Dilution of the crude antigens beyond the stock 1:100 strength greatly weakened the reaction, and it is suggested that a much stronger antigen or a purified preparation should be used. It is also suggested that the immune bodies on which dermal sensitivity and the complement fixation tests depend may not be identical and the complement fixation test should provide better diagnostic evidence of existing infection.

II. The second paper deals with the application of the complement fixation test to human sera following the technique used in the tests on guinea-pig sera. Complete complement fixation was given with 8 out of 9 sera from proved cases of histoplasmosis. 7 out of 13 sera of persons (chiefly children) who, after an earlier negative skin test result were found to have developed dermal sensitivity to histoplasmin which suggests recent infection, and 6 out of 36 sera of persons, with active pulmonary lesions who were histoplasmin positive and tuberculin-negative. Allowance should be made for the probability that

some of the sera had been collected after the specific antibody titre had fallen. Control sera numbering 242 from various sources, including 58 from persons who were histoplasmin-positive and tuberculin-negative, gave entirely negative results.

In the case of proved histoplasmosis there was a close parallel between the results of dermal sensitivity tests and the complement-fixation test.

This serological study offers the hope of a valuable additional means of diagnosis, in the complement-fixation test, and it lends support to the view, based mainly on the evidence of dermal sensitivity to histoplasmin, that histoplasmosis may exist in an undetected, subclinical form. J T Duncan

HARVEY, N A **Progressive Coccidioidomycosis Report of a Case** *Ann Intern Med* 1948, Mar, v 28, No 3, 651-61, 2 figs [25 refs]

"A case of progressive coccidioidomycosis is presented with clinical data and necropsy findings. A generalized coccidioidal peritonitis found at autopsy was apparently caused by the intraperitoneal release of infective material from necrotic liquefying nodules on the surface of the spleen and liver. The complement fixing antibodies never gave a positive test in dilutions greater than 1/8, and the patient became anergic to intradermal injections of coccidioidin (1/100 dil) in the terminal stages of the disease. A total of 6,260,000 units of penicillin was given with no demonstrably beneficial clinical effect. Many analogies can be drawn between coccidioidomycosis and tuberculosis. A brief discussion of some aspects of the disease is presented."

FURTADO T A & PELLEGRINO, J **A terapeutica da blastomicose Sul-Americana, ensaios "in vitro" com a estreptomicina** [Treatment of South-American Blastomycosis Trial of Streptomycin "in vitro"] *Brasil-Médico* 1948, Feb 21 & 28, v 52, Nos 8/9, 54-6 [20 refs] English summary

The authors show, by references to the literature, the unsatisfactoriness of the treatment of *Paracoccidioides brasiliensis* infections. They mention local injection of 10 per cent sodium iodide by Magalhães, methylene blue by Pupo, these same two drugs with sodium cacodylate by Prado, and the varying results recorded of these, the failure of tartar emetic, gonacrine, tryptaflavine, arsenicals, sulphapyridine and other sulphonamide drugs. Tyrothricin was favourably reported upon from *in vitro* experiments by Lacaz and Cury, but *in vivo* this could be used locally only because parenterally it was toxic and haemolytic. Now, the authors have tested streptomycin in dilutions from 500 microgrammes to 1 microgramme per cc on cultures in Sabouraud glucose. Twelve days later growth had been inhibited in the two strongest, partial in the 300 per cc, but not in the others and even with the first two growth took place unimpaired on transfer to fresh medium. The action is, therefore, fungistatic only, and not fungicidal.

H Harold Scott

BROCKMAN, D D **The *in vitro* Effect of Atabrine on *Cryptococcus neoformans*** *Amer J Trop Med* 1948, Mar, v 28, No 2, 295-7 [11 refs]

"Atabrine is fungicidal *in vitro* at concentrations of 25 to 50 mgm per cent and fungistatic at 3 to 25 mgm per cent for *C. neoformans*. Toxic reactions are obtained with much lower plasma or tissue concentrations. Atabrine is, therefore, of little therapeutic value in cryptococcus infections."

## TROPICAL OPHTHALMOLOGY

## A REVIEW OF RECENT ARTICLES. L

*Parasitic conditions.*—A case of Trombiculid mites on the eyelid is described by BOASE.<sup>1</sup> The skin of the lash-bearing area of the left upper eyelid presented a reddish powdery appearance. At the first glance this was thought to be red murrain dust or some form of native medicinal powder but on closer examination the dots were seen to be uniform in size individually of a bright red colour and evidently red mites. On identification, these proved to be the larvae of the genus *Trombicula*. This genus is the vector of scrub typhus in South-East Asia. The evidence in this case suggests that infestation occurred in the Ankole district of South-West Uganda.

Complete up-to-date literature of ocular sporotrichosis is reviewed by GORDON.<sup>2</sup> Forty-eight cases have been reported in the world literature. Apparently in 34 of these cases, the ocular disease was primary and in 14 secondary to involvement elsewhere in the body. In two of these cases the diagnosis was in question. Of the 48 cases, 10 have occurred in the United States of America and the majority of the remainder in France.

The disease in the eye most commonly manifests itself as ulcers of the lids and conjunctivae. These tend to begin as large subcutaneous gummas and break down to form ulcers. The latter are deep and may even develop in the bony walls of the orbit. The eyeball itself can be implicated in three ways—by direct trauma, by direct extension, or by the blood stream.

The author's case was in a woman aged 48 years, who came to the eye clinic complaining of a "sore" on her upper eyelid. There was no definite history of trauma, but about a week prior to the onset she had been working in her garden among polisetias. There were marked swelling and redness of the eyelid with a granulation ulcer in the centre. The globe and the lachrymal apparatus were not involved. A culture on Sabouraud's medium was made from the material taken by aspiration from a nodule near to the ulcer. This five days later revealed *Sporotrichum schenckii*. The patient was treated with a saturated solution of potassium iodide. The initial dose was 10 drops four times a day. This dose was gradually increased up to 25 drops four times a day and she responded well to treatment. The average period of medication is from one month to six weeks.

*Trachoma.*—The treatment of 600 cases of trachoma by sub-conjunctival injections of sulphonamide is discussed by BIZANT.<sup>3</sup> These comprised the very early cases, those in the follicular stage, those with acta, a corneal complication, and those with scar tissue formation. The results were excellent.

He has formed the following conclusions:—The accompanying conjunctivitis rapidly disappears. The usual distressing symptoms quickly improve or disappear, the follicles on the tarsal conjunctiva smooth down and become less prominent. In corneal trachoma the improvement is very marked and rapid. Ulcers and abscess of the cornea with hypopyon become improved after the first injection, the cornea losing its angry appearance with rapid clearing up of the zone of infiltration and cicatrization occurring after a few days. Lannus crassus becomes less intense and quickly smoothes down and retrogresses. Diffuse opacities of the cornea become less in extent, the cornea becoming more

<sup>1</sup> For the 47th of this series see Vol. 45, pp. 1043-1045.

BOASE, A. J. Trombiculid Mites on Eyelid. *East Afr. Med. J.* 1947, Oct. 24, No. 10, 363.

GORDON, D. M. Ocular Sporotrichosis. Report of Case. *Arch. Ophthalmology* 1947, Jan. 37, No. 1, 54-72, 3 figs. (1 in colour). 46 refs.

BIZANT, P. Essais de traitement de trachome (par cas, par de injections sous-conjunctivales de sulfonamide thioribide). *Bull. Soc. Path. Exot.* 1947, 4, No. 7, 277-84.



transparent with considerable improvement of vision in many cases. Those cases with xerosis and infections of the uveal tract show no improvement.

In the ordinary cases, there are no contra-indications to the use of the drug. Pain sometimes occurs, especially after the first injection and occasionally a slight haemorrhage appears after the injection.

The dosage recommended is  $\frac{3}{4}$  to 1 cc of the solution. [No mention is made of the exact composition of sulphonamide used or the strength of the solution.]

**Leprosy**—The effect of Grenz rays on leprous infiltrations on the anterior portions of the eyeball is discussed by SÄGER and MITERSTEIN<sup>4</sup>. Lepromas on the bulbar conjunctiva close to the limbus are somewhat amenable to local therapy, unless the process has penetrated too far into the eye or originates from the ciliary body. The usual treatment of these lepromas consists in the application of solid carbon dioxide, the local injection of various drugs, and surgical measures. In previous experiments with irradiation, it was found that cutaneous lepromas were noticeably affected by the Grenz rays and the results were fairly good.

The authors treated 6 patients in whom there were lepromatous changes in the anterior segments of the eyeball. Three practically sightless eyes were first exposed to these rays and in all 3 patients the lepromas became reduced in size or disappeared completely. When the Grenz rays were employed on the eyes of 3 additional patients which presented lepromas with fairly good vision, two eyes exhibited a favourable response, and in the third the lepromatous part became quiescent or even slightly flatter, while the surrounding parts presented rapid growth of new lepromas. The voltage of the rays used ranged from 6 to 14 kilovolts, which is equivalent to half value layers of 0.021 to 0.031 mm of aluminium. The most effective doses applied at one sitting were from 700 to 1,200 k, the total amount varying from 5,500 to 11,600 k.

These large doses could be applied safely to the external tissues of the eye, because the sensitivity of such tissues to rays is lower than that of the skin. No damage to the cornea, lens or deeper structures of the eye was noted, so far as this could be determined on the basis of observations extending over a period of between two and four years.

**Optic neuritis**—A case of tryparsamide optic neuritis treated by 2,3 dimercaptopropanol (BAL) is reported by FRIEDENBERG<sup>5</sup>. The case was one of tabes dorsalis due to syphilis which was treated for six months with intramuscular injections of sodium iodobismuthite and a course of penicillin. These were followed by two intravenous injections of 0.7 gm and 1.0 gm of tryparsamide at a week's interval between the injections. Two days after the second injection the patient complained that he could not see the sidewalk when walking. Examination confirmed the loss of the inferior visual fields and that he was suffering from optic neuritis. He was at once put on BAL therapy. The first two days he was given 300 mgm twice daily and the following eight days he was given 300 mgm daily with the exception of the fifth day, when 400 mgm were given. Several hours after this injection he complained of paraesthesias in the left side of his neck and jaw. This lasted about one hour. Vision returned nine days after BAL therapy was stopped. On examination six months later the visual fields showed great improvement and the acuity of vision remained normal. The author is of opinion that the unusually rapid return of vision was probably due to the prompt use of BAL as soon as the patient complained of visual disturbance.

<sup>4</sup>SÄGER F & MITERSTEIN B. Effect of Grenz Rays on Leprous Infiltrations. III. Response of Lesions of the Anterior Portions of the Eyeball. *Arch Ophthalmol*, 1947 July, 38 No 1 78-88 [fig. 113 refs.]

<sup>5</sup>FRIEDENBERG S. Tryparsamide Optic Neuritis treated by 2,3 Dimercaptopropanol (BAL). *J Amer Med Ass* 1947 Dec 29, 135 no 16 972

splenectomy was done for traumatic rupture and in five for splenomegaly. In both the patients with traumatic rupture a quiescent period, lasting in one case for three days, preceded the onset of acute symptoms.

W. L. Harnett

ELMES, B. G. T. & BALDWIN, R. R. T. Malignant Disease in Nigeria: an Analysis of a Thousand Tumours. *Ann Trop Med & Parasit.* 1947, Dec. v 41, No. 34, 321-8, 4 figs. on 2 pls. [13 refs.] [Summary appears also in *Bulletin of Hygiene*.]

In a paper published in 1934 and abstracted in this *Bulletin* (1935, v 32, 522) SMITH & ELMES gave a detailed analysis of 500 consecutive malignant tumours which had arisen in Nigerian Africans and had been submitted to pathologists in that country for identification. The present paper is a summary of 1,000 additional tumours from the same source. The tumours correspond in nature and incidence fairly closely with those recorded in the earlier paper. The youth of the patients is again noticeable, 248 of the 1,000 having been under thirty years old. Of all the tumours 81 per cent. began in the liver and were associated with subacute necrosis and cirrhosis of the Larnec type. Attention is specially drawn to those conditions in which the causation is not entirely obscure. Among these besides the liver cancer which are largely due to erroneous feeding, are many epitheliomas growing in leg ulcers, five cases of scrotal cancer and ten of cancer of the penis. Of 18 instances of malignant disease of the bladder only four were accompanied by *Schistosoma haematobium* infection, despite the frequency of this malady in Nigeria. Notable features among the thousand tumours analysed are the relative frequency of melanoma (6.5 per cent.) mixed salivary tumour (4.9 per cent.) and adamantinoma (1.8 per cent.). The paper though brief, contains several other items of interest and should be read in the original.

Harold Burners

## PROTOZOOLOGY GENERAL

HEAL, B. H. & GROCOTT, R. G. Congenital Toxoplasmosis. *J Amer Med Ass.* 1948, Jan. 10, 136 No. 2, 104-8, 11 figs. [Refs. in footnotes]

The case described was in an infant prematurely born after 6½ to 7 months of pregnancy. The infant died 10½ hours after birth. A post mortem was performed 31 hours after death, the body having been kept in the refrigerator at a temperature of 33 to 38 F. The brain was a collapsed gelatinous mass and was covered by haemorrhagic leptomeninges. Histologically areas of focal necrosis with extensive deposition of calcium salts occurred. The eye showed extensive chorio-retinitis. Toxoplasma were found in the brain, eye and many other organs. Inoculated with brain material, guinea pigs acquired an infection which was maintained by sub-inoculations. Attempts to demonstrate a latent infection in the mother failed, but a serological precipitation test was not carried out. This is the first case of congenital toxoplasmosis to be described from Panama.

C. M. H. Cuyon

RICHMAN, I. Occurrence of Toxoplasma Neutralizing Antibodies in various Disease Conditions. *J Lab & Clin Med.* 1948, Jan., v 73, No. 1, 67-68, 13 ref.

The toxoplasma neutralization test of GANIX was employed to determine the presence of antibodies in various diseases. Of the sera from 77 selected individuals, twenty were positive, forty-eight negative. A few doubtful. This

was a high incidence of positive sera amongst children showing signs of congenitally acquired toxoplasmosis—convulsions or other signs of central nervous system involvement and hydrocephalus or microcephalus when these were associated with chorioretinitis or cerebral calcification. The blood of the mothers of such patients regularly showed antibodies. Antibodies were also found in a child with prolonged encephalitis and in two adults with mental disturbances. The antibodies persist in the blood stream for at least five years. Many conditions of obscure aetiology failed to show the presence of antibodies.

C M Wenyon

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## ENTOMOLOGY AND INSECTICIDES GENERAL

MACKERRAS, I M The Jackson Lecture Australia's Contribution to our Knowledge of Insect-borne Disease *Med J Australia* 1948, Feb 7, v 1, No 6, 157-67 [Bibliography]

The lecture gives a readable general account of the development of our understanding of insect-borne diseases. It pays particular attention to Australian problems and the work carried out in that continent. It gains much because the author has a first-hand knowledge of some parts of the work and also because of the excellent list of selected references. Like many other general papers, it is difficult to summarize.

The author gives a general classification of his subject, pointing out that there are many different types of relationship between the arthropod and the mammal. He then develops the subject historically under three periods. In the first of these, most of the major discoveries were made and the period might be said to be one of zoological observation. So far as Australia is concerned, it started in 1876 with the discovery by Joseph Bancroft of the adult nematode which was called *Filaria bancrofti* by Cobbold. This first period ended at about the year 1900.

During the second period, which occupied the first twenty-five or thirty years of this century, few major discoveries were made except in the life histories of rickettsiae, but results worked out in one area were plotted or confirmed in many other parts of the world, and the sciences of parasitology and medical entomology may be said to have been established. During this period, Australian workers made important contributions to knowledge, particularly the relation to plague, dengue and filariasis. They also carried out most useful surveys of the parasites of Australian vertebrates.

In the third period, which commenced between the world wars, experimental and physiological studies were developed, founded on the earlier observations, so that there was a great elaboration of technique. In medical entomology, ecology and the closely related science of epidemiology began to take a large place. Australian workers covered a wide field. One might perhaps refer particularly to their virus research and that on infections of the typhus group, which became of such importance during the war period. Here the author records with legitimate pride that it was an Australian who brought in the use of the phthalates to kill the *Trombicula* and showed how they could be applied in the field. Outstanding Australian work on many sides of malaria must be familiar to all. It is less well known that when an epidemic resembling dengue appeared in jungles in New Guinea, it was shown that the infections were carried by a jungle mosquito *Aedes scutellaris*, infected material being taken by air to Australia where the experimental proof was completed.

P A Buxton

FERGUSON M. S. & GRAHAM O. H. *Phlebotomus* in New Guinea and Nearby Islands. *Trans. Roy. Soc. Trop. Med. & Hyg.* 1948 Mar v 41 No. 5 679-84 2 figs.

Adults of *Phlebotomus* as yet undescribed, were collected from tree holes, trunks and buttresses. For the collection of living sandflies, tobacco smoke was used. Later the Freon aerosol bomb was employed and the flies fell on to a white cloth and died. No *Phlebotomus* were taken in fox-holes or in pill-boxes. Fallen trees and light traps yielded none though other members of the family were sometimes numerous.

A table is given of the data concerning the collections and a map shows where the collections were made. The rôle played by *Phlebotomus* in the transmission of disease was not determined. It is expected that descriptions of these sandflies will be published in due course. H. S. Lleson

BRENNAN J. M. An Instance of the Apparent Toxicity of Man to Ticks. *J. Parasitology* 1947 Dec., v 33 No. 6 491-4

The man to whom this paper relates was apparently perfectly healthy, scrupulously clean, exceptionally hairy, and was not addicted to narcotics or alcohol. His only excess was to drink as many as 20 cups of coffee each day. Adult ticks (*Dermacentor Andersoni* and *Imloffiana americana* n. sp.) held in contact with his skin (in the antecubital fossa) for some 10-40 minutes, were always rendered immobile. They revived within 24 hours but never became quite normal. Nymphs of *D. Andersoni* held in the same place or in the closed hand were killed in 3-10 minutes. Controls on other persons were entirely unaffected.

On the other hand, adult ticks and nymphs applied to parts of the skin free from sweat behaved irregularly, some were affected and others not. Ticks held near the skin but not on it were not affected. It was not possible to collect a quantity of sweat sufficient for a real test, but ticks placed inside a rubber glove worn by the subject of the experiment and containing a trace of sweat were not affected. His urine was harmless to them.

The ticks were obviously repelled, as well as intoxicated. It seems likely that there is some substance, presumably associated with the man's sweat which is both toxic and repellent. The condition is rare since no suggestion of it was found in 70 volunteers to whom ticks were similarly exposed. If this substance could be isolated, results of far-reaching value might be obtained.

Charles H. Woods

HIRANT H. & BAUR, O., M.D. Sur la présence en France de *Dermacentor noui* (Neumann, 1897). [The Presence in France of *Dermacentor noui* (Neumann, 1897)] *Bull. Soc. Path. Exot.* 1947 v 40 Nos. 11/12, 463.

The authors found a male specimen of *Dermacentor noui* on the scapular region of a Mongolian child of 5 who was under treatment in the neighbourhood of Lodève (Hérault). This child had a continuous fever of 39° to 40° C. on the day of examination and on the five following days. No other signs, cutaneous or visceral, were found in the patient.

The common hosts of *D. noui* are the sheep, camel and wild boar. It is possible that the tick was dropped from some animal in the meadows where the child was accustomed to play. It is evident that although as far as the authors are aware this species has not been reported from France before, it does occur, can attach itself to man and had a possible bearing on the febrile attack of the child who accidentally acquired it.

The authors assume that *D. niveus* cannot be regarded as a simple variety of *D. reticulatus* (Fabricius, 1794) a species well known in Europe and commonly known to-day as *D. marginatus* (Sulzer, 1776)

H J O'D Burke-Gaffney

GARNHAM, P C C The New Insecticides East African Med J 1948, Jan, v 25, No 1, 5-10

This paper discusses the use of DDT and Gammexane and particularly describes experiments carried out in recent years in East Africa in the control of insect borne diseases The use of the newer insecticides in the control of malaria, relapsing fever and onchocerciasis is described, the results of relevant experiments have already been abstracted in this *Bulletin* from time to time The author also gives a brief description of the use of these insecticides in the control of *Aedes aegypti* and of common domestic pests

H J O'D Burke-Gaffney

DRESDEN, D & KRIJGSMAN, B J Experiments on the Physiological Action of Contact Insecticides Bull Entom Res 1948, Feb, v 38, Pt 4, 575-8 [12 refs]

The toxicity of an insecticide to an insect or vertebrate can be determined from external applications or by injection into the body cavity Data obtained by other workers are summarized and further results obtained by the authors with a cockroach a stick insect and a frog are tabulated According to these comparisons, the internal toxicity of DDT, Gammexane and Rotenone are of the same order to vertebrates and to insects But the vertebrates require much higher external doses, showing that their skins are effective barriers to this type of poison, whereas the insect cuticle is readily penetrated

The toxicity to *Periplaneta* of the various isomers of hexachlorocyclohexane was investigated It was found that, even after injection, the gamma isomer is outstandingly effective, its toxicity, therefore, is not due merely to its ability to penetrate the cuticle

In view of the suggested connexion between Gammexane poisoning and meso-inositol, tests were made in which cockroaches were injected with both separately and with various mixtures The inositol (which was itself innocuous) showed no sign of reducing the toxicity of the Gammexane

J R Busvine

JONES, B M Preliminary Tests of DDT Emulsion Concentrates Bull Entom Res 1948, Feb v 38, Pt 4, 585-90, 2 figs

The following emulsion concentrates were tested, Nos 1, 3 and 4 "soluble oil" type, No 2 "mayonnaise" type Nos 1 and 2 had solvent naphtha as a solvent for the DDT whereas Nos 3 and 4 had a toluene-turpentine mixture The DDT content of these concentrates ranged from 23 to 30 per cent

A simple test of stability was to prepare 1 per cent DDT emulsions from all concentrates and to observe how soon the emulsions would break Nos 1 and 2 were stable for twenty-four hours, but Nos 3 and 4 separated into two layers in thirty minutes and had broken in twenty-four hours The initial separation of Nos 3 and 4 was delayed by the normal agitation of a man using a knapsack sprayer Attempts to prepare 1 per cent dilutions with salt water (4.5 per cent salinity) were only successful with the "mayonnaise" formula

As a small field trial two rooms were sprayed with emulsions diluted to 5 per cent from concentrates Nos 1 and 2, to give about 200 mgm DDT per sq ft Mosquitoes (*Anopheles obturbans* and *Culex gelidus*) were liberated in the

treated rooms, for various periods, at intervals up to sixty days after treatment. The exposure necessary to produce 100 per cent. kill rose from about an hour to ten hours, but the loss of activity was not more rapid than with a kerosene-DDT treatment.

J. R. BARNES

BRENNAN J. M. Field Tests with Tick Repellents. *Pub. Health Rep. Wash.* 1948, Mar 12, v 63 No. 11 338-48.

Field trials of tick repellents were arranged by the Rocky Mountain Laboratory, Hamilton, Montana, in collaboration with the U.S. Army. Men wearing fatigue kit were exposed to heavy attacks of *Amblyomma americanum* for about four hours per day for eight days in one trial and for ten days in another trial. The uniforms had been impregnated with one or two ounces of the various repellents (a pair for each treatment and four controls). Ticks acquired were removed and counted at intervals. The results are a little difficult to interpret because some of the treatments were more effective than others at first but did not last so well. Some were only highly effective against nymphal ticks while others were also good against the adults. However the following conclusions seem justified --

From the standpoint of maximum repellency butylacetanilide and benzyl cyclohexanol were first and second in all tests. Butylacetanilide also showed indications of promise as a mite (chigger) repellent. Although there are no data regarding its toxicity to mammals it is known that related compounds are harmless. There were no adverse reactions in the soldiers who wore the impregnated clothing.

Benzyl benzoate and dimethyl phthalate were also included in the tests. They gave rather erratic results especially against adults, but their repellence was fairly high and in view of their availability and safety they should be used against ticks at present.

Dibutyl phthalate and the "6 2 2" mixture gave rather poor results against ticks. (The "6 2 2" mixture contains 60 per cent. Dimethyl phthalate 20 per cent. Indakone 20 per cent. - ethyl-1,3-hexanedithiol.)

J. R. BARNES

## REPORTS SURVEYS AND MISCELLANEOUS PAPERS

ROSS INSTITUTE OF TROPICAL HYGIENE. LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE. Report of the Eighteenth Meeting of the Ross Institute Industrial Advisory Committee, 6th January 1948. [WIGGLESWORTH A. Chairman] 23 pp. 1 diagram

This is an account of a meeting at which the chairman, Mr. Wigglesworth referred to the opening of the new branch of the Ross Institute at Tanganyika Territory. A paper was read by Dr. TREDDER on the East African labourer in which he remarked that 90 000 men are employed on estates in Tanganyika, half of them round Tanga. These men suffer much from malaria, hookworm infestation and anaemia, and are often underfed. A haemoglobin content of only 60-70 per cent. is not uncommon in men who make no complaint of illness. Although the Government have laid down a minimum allowance of 2,600 Calories for labourers, it is not possible to be sure that each man gets the amount in full, or prepares the food adequately for consumption.

Papers on the eradication of *S. malinse* from streams in Kenya, by the use of DDT and on mass treatment in the control of schistosomiasis in Southern Rhodesia, were read by Dr. GARNHAM and Mr. ALVES. Papers on these subjects

have already been reviewed in this *Bulletin*. Alves makes the important point that the opening up of African water supplies for hydro-electric, irrigation or even domestic use, will mean corresponding extension of the area in which the schistosome-bearing snails are to be found, unless the engineers seek the advice of public health workers from the start [It would be impossible to over-rate the importance of this]

*Charles Wilcocks*

COLONIAL OFFICE **Inter-University Council for Higher Education in the Colonies**  
**Report 1946-47** [IRVINE J. C., Chairman] Cmd 7331 12 pp 1948  
 London H M Stationery Office [3d]

GABUS, J. **Organisation et premiers résultats de la Mission ethnographique chez les Touaregs soudanais du 26 décembre 1946 au 10 mars 1947** [Preliminary Report of the Ethnographic Mission to the Tuaregs of the French Sudan in 1946-47] *Acta Tropica* Basle 1948, v 5 No 1, 1-56, 5 maps 11 figs & 16 photos

INDIA **Annual Report of the Public Health Commissioner with the Government of India for 1945** [COTTER, E.] pp iv+91, 2 folding maps & 8 charts 1947 Delhi Manager of Publications [Annas 14 or 1s 3d]

This report is described as being more or less on the same lines as those of the years immediately preceding the war, it contains considerably more information than was provided for the years 1941-1944, but, on the other hand, certain items are omitted because they have already appeared in a preliminary note published earlier in the year (1947)

In spite of the war, some progress can be reported for example, certain provinces introduced compulsory inoculation against cholera for persons desiring to attend the religious "fairs" which had hitherto played so great a part in disseminating infection

The birth rate for 1945 was 27.3 *per mille* against 25.4 in 1944 and 32 to 34.5 during the five years 1937-1941

The death rate was 21.5 *per mille* against 24.1 in the previous year and 21.1 to 24.3 during the period 1937-1941. In Orissa the death rate was slightly higher than the birth rate and in the Central Provinces both rates were about 39 *per mille*. In the Punjab the birth rate (about 37) was nearly twice as high as the death rate (19.5)

The infant-mortality rate was 150.9, the lowest ever recorded, but there again there are surprising differences, for example, the rate in the central Provinces was 256.6 whereas in Bihar it was less than 100 although in the latter province the total death rate was nearly the same as for British India as a whole

It must be understood that all the vital statistics for India are quite unreliable, local checks have repeatedly shown that many births and deaths, especially infant deaths, have not been reported. It is disquieting to find that in a Health Unit in Madras dealing with a population of about 50,000, the infant-mortality rate was 236 despite the fact that for several years the area had been provided with a special health staff, including trained midwives

In several provinces deaths from cholera and smallpox were more numerous than for many years past but although these diseases attract special attention because of their dramatic nature, taken together they were responsible for only about one-fifteenth of the deaths in British India as a whole. Readers of the report will be surprised at the statement that Bengal was "only mildly" affected by cholera, the deaths from the disease having been 32,550

Vaccination against cholera was practised on a large scale in most of the affected areas, the numbers of inoculations were in Bengal 7½ million,

in Bihar nearly 6 million. In the Central Provinces, Bombay and Madras about 2 million each.

The incidence of plague continued to decline except in Bombay Province where there were 11,779 deaths against 514 in 1944. The preventive value of DDT which was released for use during the year was being investigated.

Malaria was not unusually prevalent during the year. It is interesting to find that "although there is some prejudice in favour of quinine, mepacrine is now becoming quite popular. Fears are expressed that control by DDT may be too costly for general adoption."

As usual the information regarding the prevalence of the enteric group of fevers is meagre, but it is stated as being "fairly certain" that no epidemic occurred during the year. [The most likely explanation of the absence of epidemics in India is that infection is so widespread that most of the children suffer from attacks which are regarded as "simple fever" so that the adult population are relatively immune.]

Pulmonary tuberculosis is believed to cause 500,000 to 800,000 deaths every year but accurate information on the subject is not yet available. Chronic malnutrition is mentioned as one of the chief factors contributing to the prevalence of this as well as of most of the other diseases included under the headings fevers and all other causes which are shown as the causes of about three-fourths of all the deaths that occur in India.

Kala azar is believed to have increased slightly in Bengal and Assam during the year. This is the one disease in India that is being kept under a reasonable degree of control, thanks to the popularity of the effective treatment available in the endemic areas.

A brief summary is given of the important Report of the Health Survey and Development Committee which was completed during the year (see this *Bulletin* 1947 44 25.) Strangely enough no mention is made of the remarkable fact that all but two of the 25 members of this fully representative Committee subscribed to the view that "the growth of population will become an increasingly serious problem and that even if economic productivity is developed to the greatest possible degree "uncontrolled growth of population must as far as we can see outstrip the productive capacity of the country. This view was reached by the Committee after a long and careful study of the available evidence its bearing on the public health policies of all the crowded and backward countries of the world is of crucial importance."

The rest of the present report is on the usual lines. It deals with the work of the official and voluntary health organizations and with medical research which continues to progress far more rapidly than the practical application of the discoveries made by the investigators. The graphs which illustrate the report are very helpful, though necessarily they are no more reliable than the statistics on which they are based.

J. K. B. D. Megee

1. *Statistical Appendices to Annual Reports of the Public Health Commissioners with the Government of India for the Period 1940-1944.* pp. ii + 177. 1947. Sarda. Manager Government of India Press for Manager of Publications Delhi. (R 24 nos 8)

EAST AFRICAN MED. J. 1948 Jan. v. 23 No. 1 29-31. The Case for the Appointment of a Royal Commission on Health and Population in His Majesty's Dependencies in Africa. Memorandum by the Council of the Kenya Branch of the British Medical Association.

The authors of this long document evidently feel strongly that the time has now come (and is probably overdue) when much more radical and energetic steps must be taken to promote the welfare of the whole population of East



Africa, than have hitherto been considered. They base their argument on the fact that the population is increasing at a rapid rate (some 12 millions in 1936 increasing at a not impossible rate of 2.3 per cent per annum would exceed 18 millions in 1956), and on the other fact that the fertility of the soil is being reduced, largely by inefficient agricultural methods. This problem is by no means peculiar to Africa, and is more and more engaging the attention of medical men and administrators in various parts of the world [see this *Bulletin*, 1945, v 42, 506, 507, 1946, v 43, 81, 603, 1947, v 44, 252, 1948, v 45, 215]. The case made by the authors is very strong indeed, though the reader may think that it would have been even more telling if it had been made much more succinctly.

The memorandum is divided into a prefatory note and two parts. Part I contains the proposal for a Royal Commission, and a discussion of the modern conception of health, which is based very largely on the ideas inherent in the Report of the National Health Services Commission, Union of South Africa, 1944, and on the papers by PATERSON on a population policy for East Africa [see this *Bulletin*, 1948, v 45, 124].

Part II contains a section on planning, in which the authors stress the fact that information on most of the matters relevant to schemes for improvement, is scanty and inaccurate. There is reason to believe that the health of the people of East Africa is deteriorating, and it is known that some parts of the country are so overcrowded that thinning of the population is becoming urgently necessary. The position will probably continue to deteriorate unless a bold effort is made to cope with it. Quotations are given from speeches and reports made by government officials, which support this contention and which show that the position is known in official quarters. The old structure of African society, based on family units and unlimited land, is breaking down in the face of industry, poverty of the soil and crowding.

The health services are inadequate, and must eventually be supported largely by qualified and trained Africans, but in the meantime such medical and public health services as are possible must be developed—but a long-term plan is needed.

The argument for a plan for East Africa is very strong, the suggestion of a Royal Commission may be the best approach to a situation so difficult that it may well be beyond the power of the countries chiefly concerned to deal with it unaided.

*Charles Wilcocks*

COONOR. Pasteur Institute of Southern India, Coonoor. Annual Report of the Director together with the Fortieth Annual Report of the Central Committee of the Pasteur Institute Association 1946-47. 50 pp, 1 chart. 1947. Madras. Diocesan Press.

The Pasteur Institute of Southern India is a private institution founded in 1906 and governed by a representative committee of its own. While its main object is to provide measures for the prevention of rabies and to undertake research and propaganda in connexion with that disease, it also provides for general laboratory and research work in that part of India. The Institute also gives facilities for research financed from other sources, the Nutrition Research Laboratories of the Indian Research Fund Association has worked there for many years and the Southern India Branch of the Research Section of the Malaria Institute of India worked there during 1946.

Much of the report is naturally devoted to reports and statistical statements regarding rabies and antirabic measures. It is noted that 20,601 patients were treated at the Institute and at Subsidiary Treatment Centres during the year

are met with—careful research and inquiry would probably discover more—in which the primary condition is lepromatous and then, after a long interval, the lesions regress and even disappear leaving scars, and give place to the neuro-cutaneous form secondarily. There were only two such in the authors' list. A photograph of one of them is given and photomicrographs to show the histology of sections of the skin.

To sum up the work is a very careful and detailed one might with justice call it a complete study of this aspect of leprosy. There are 109 illustrations all clearly reproduced and showing what the authors describe in the text. The matter is well arranged, the clinical records aptly chosen and quotations fully authenticated. Each chapter has its references in footnotes and these are abundant. In short, this is an admirable piece of work and should be in the hands of all leprologists interested in the clinical and pathological aspects of tuberculoid leprosy. There is no index, but the contents of each chapter are given at the beginning of the book and also at the head of each chapter so that a detailed index is not really needed.

*H. H. and Scott*

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# TROPICAL DISEASES BULLETIN

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## SUMMARY OF RECENT ABSTRACTS\*

### VII HELMINTHIASIS

#### *Trematodes*

*Schistosomiasis, general*—COWPER (p 217) has written on the maintenance and breeding in Britain of snail hosts of schistosomes, for details the original should be consulted

MUKERJI *et al* (p 599) have been unable to transmit *S haematobium* and *S mansoni*, from African troops, through the common Indian snails

KHALIL and HILMY (p 97) describe a palm-leaf snail trap which is used in Egypt to measure the intensity of snail infestation in water-courses before and after eradication has been attempted. For details the original abstract should be consulted

BARLOW and ABDEL AZIM (p 831), reporting on the control programme in Egypt, make the point that winter closure of irrigation canals causes a high proportion of infected snails to die. Copper sulphate is used, and the authors (p 832) state that there is no advantage in using lime and other chemicals which they have tested. The use of palm-leaf traps in streams lacking vegetation is advantageous. They report considerable reductions in stream infestation as a result of the various measures taken. In experimental work, no infection was achieved with cercariae 48 hours old (compare ALVES below)

Gammexane is lethal to *Bulimus* and *Planorbis* in Egypt in concentrations of 5-6 p p m acting for 24 hours. HALAWANI (p 331) thinks that much smaller doses would suffice if applied for a longer time. The same author (p 667) claims that the *delta* isomer of benzene hexachloride is effective against *Bulimus* and *Planorbis* in a dilution of 5 parts per million

*Schistosoma haematobium*—STEPHENSON (p 598) describes the schistosomiasis position in the Gezira area of the Sudan, where the land is irrigated from the great dam at Sennar. There are 2,600 miles of irrigation channels, some of which are used only by day, others throughout the 24 hours. There has apparently been a great increase in the infestation rate with *S haematobium*, and 21 per cent of adults and 45 per cent of children are infested. *S mansoni* is present in 5 per cent in some places, but no one method of stool examination will reveal all cases. The position seems to be deteriorating, and treatment

\* The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin* 1947 v 44. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed

campaigns, construction of latrines, siting of villages away from canals, and propaganda have not succeeded in controlling the disease. Snail-clearance as practised in Egypt, is needed.

BUCKLEY (p. 909) has made a survey of N Rhodesia in which he found *S. haematobium* infection in up to 60 per cent. of the people children showing higher figures than adults. *Physopsis globosa* and *P. africana* are the snail hosts they are essentially inhabitants of small streams, and are scarce in large rivers lakes or swamps.

MAKAR (p. 1010) writes on the pathology and treatment of carcinoma of the bladder in Egypt which is probably associated aetiologicaly with *S. haematobium* infection. Other papers on schistosomiasis and cancer have been written by SCANDER BEY (p. 1010) OXSEY BEY (p. 1011) and MAKAR and FAWKY (p. 1011).

ALVES and BLAIR (p. 823) describe the preparation of an antigen from cercariae of *S. haematobium*. This is used for the intradermal test and is valid for *S. haematobium* or *S. mansoni* infections. In a large series of persons tested, there were no negative results in those excreting eggs, and eggs were found in a large proportion (increasing as examinations were repeated) of those with positive tests to this antigen. The authors therefore consider the test to be accurate enough for diagnostic use in mass treatment campaigns in S. Rhodesia, where the intensive treatment with sodium antimonyl tartrate is practised. Negative reactors are probably free from the disease.

A description of the field work done during 1948 in S. Rhodesia is given by ALVES and BLAIR (p. 827) who by the intradermal test referred to above have found infection in 4-41 per cent. of Europeans and 13-89 per cent. of Africans. They treated 5455 infected persons by intensive courses of sodium antimonyl tartrate (total dose 1 grain to 20 lb body weight divided into 3 parts and injected in very dilute solution and very slowly at intervals of 3 hours). There were no deaths from the drug, but the technique of administration is of the greatest importance. For snail control they used copper sulphate, of which a concentration of 5 p.p.m. kills all snails in 4 hours in the laboratory it is much more effective than malachite. The control work should be done in the dry season in S. Rhodesia.

ALVES (p. 829) reports that GORMAN has discovered that schistosome cercariae may live as long as 44 hours in cold weather and be infective for fish. The old idea that by storing water for 48 hours, free from snails, it is rendered harmless for schistosomiasis cannot now be accepted.

SEITZ (p. 829) has treated 327 patients, mostly with *S. haematobium* infection, by an intensive method similar to that used by Alves and Blair without serious reaction, and with good results.

BARTER *et al* (p. 1012) show that blood levels of tartar emetic fall very rapidly and that excretion by urine (80 per cent.) and faeces (20 per cent.) is rapid. Experience with multiple injections suggests that it is possible to maintain a higher blood level by controlling the size and frequency of doses.

HALAWANI and ABDALLAH (p. 220) gave Repodral (an American preparation identical with Fouadin) 3 times a day for 2 days to Egyptian patients with *S. haematobium* infections, with some success. The total dose was 0.5 cc. (of 0.3 per cent. solution) per kgm. divided into 3 parts. This intensive treatment is probably safer than the intensive treatment with tartar emetic in view of the prevalence of biliary cirrhosis and nutritional deficiencies in Egypt. (The Repodral was presumably given by intramuscular injection, but this is not made clear by the authors. HAYMOUDA (p. 221) examined the hearts of these patients by electrocardiography but any changes found were slight and transient. HALAWANI and HASSI (p. 329) prepare a 0.5 per cent. solution of Repodral solution immediately before use. This solution should be used on the day of preparation. Toxic symptoms are generally mild. EL AYADI

(p 433) shows that after an intensive two-day course of Reprodral (Fouadin, Stibophen), much of the antimony was concentrated in the liver. A cumulative effect was clearly demonstrated. GELLHORN *et al* (p 334) discuss the tissue distribution and excretion of certain organic antimonials in hamsters, for details the original should be consulted.

RITCHKEN and KANTOR (p 1078) report a few cases of herpes zoster in patients treated by the intensive course of intravenous antimony injections, they discuss its aetiology.

WOOD (p 914) reports on the pharmacology of Miracid, the new drug which is claimed to be active against schistosomes.

*S. mansoni*.—In N Rhodesia BUCKLEY (p 909) found *S. mansoni* in up to 61 per cent of people. In general the areas of high incidence with *S. mansoni* were not those with high incidence of *S. haematobium*, and children were not specially affected. It was common to find eggs in faeces without blood or mucus, and the disease appears to be very insidious. The snail host is probably *Biomphalaria pfeifferi*, evidence regarding the closely allied *B. tetragonostoma* is inconclusive. These snails are found in small streams, but are scarce in lakes and swamps.

SCHWETZ (p 1009) found that about 10 per cent of 317 persons examined along the Bushumale river in the Belgian Congo had intestinal schistosomiasis, and found *Planorbis adowensis* and *Bulinus forskali* in the neighbourhood.

SCHWETZ and DARTEVELLE (p 825 bis) discuss the snail hosts of *S. mansoni* in the eastern part of the Belgian Congo, and give some information on their ecology. [In the original abstracts *Planorbis boissyi*, *tanganikensis* was misspelt *tanganikus*].

RODRIGUEZ-MOLINA and SCHWACHMAN (p 829) found *S. mansoni* in 14.6 per cent of a large number of recruits in Porto Rico. They treated a number with Fouadin, but the end results after 24 months were not good—more than half the men still excreted eggs, though some of them had had as many as 6 courses of the drug. PONCE PINEDO (p 826) reports the first known autochthonous cases of *S. mansoni* infection in the Republic of Santo Domingo.

LUTTERMOSER (p 1078) has contributed a comprehensive account of schistosomiasis in Venezuela, where the disease is well established in certain States. The snail host is *Australorbis glabratus*, and in the programme of control, treatment, drainage of land, application of lime and other chemicals to kill snails and the development of good methods of disposal of faeces are prominent features.

JAFFÉ and FERRO (p 433) discuss the diagnosis of schistosomiasis in post mortem material in Venezuela, comparing different techniques for the demonstration of ova in liver and rectum. By various means they obtained positive results in 34 of 86 cadavers.

*S. mansoni* infection is very widespread in Brazil, PINTO and DE ALMEIDA (p 96) give a list of 198 foci already found, chiefly in the State of Pernambuco. CANÇADO (p 912) reports on the distribution of *S. mansoni* in the State of Minas Geraes, Brazil.

PINTO (p 216) relates a focus of *S. mansoni* infection near Rio de Janeiro to watercress gardens contaminated with human faeces and harbouring *Australorbis glabratus*. PINTO and DE ALMEIDA (p 216) give a list of other occupations which carry special risk—washerwomen, workmen building bridges, engineers, topographers, fishermen, and persons, young and old, who break down the *guaxima* tree for fibre, standing in water to do so. The snail hosts in Brazil are *A. glabratus* and *A. olivaceus*.

CRAM and FILES (p 217) have confirmed previous findings that a species of *Tropisorbis* found in Louisiana is capable of acting as host for *S. mansoni*, various other species tested could not be incriminated. In an investigation of

a number of species of snails found in the Eastern United States, while STUNKARD (p. 432) attempted to infect with the three human schistosomes, no evidence was found that any could act as an intermediate host for any of the trematodes.

Snails normally liberate cercariae once each day around midday but KIRK (p. 330) has been able to force *A. glabratus* to shed cercariae of *S. mansoni* more often, by exposing them to various intensities and periods of light, and to different temperatures. Abrupt changes in temperature exert more influence than abrupt changes in light intensity.

HASHEM (p. 730) discusses Egyptian hepato-splenomegaly which is endemic in an area roughly corresponding to that of *S. mansoni* infection. In all cases at post mortem, in which eggs could be differentiated in the liver they were eggs of *S. mansoni* and this trematode is the cause of the condition four times as often as *S. haematobium*. In schistosomal cirrhosis the fibrosis is essentially interstitial, and is due to infiltration in and around the fine portal tracts by eggs or even adult worms. ESPAN (p. 913) describes the pathology of the liver in schistosomiasis in Egypt eggs of *S. mansoni* are found more than 4 times as often as eggs of *S. haematobium* in hepatic schistosomiasis. He also describes the symptoms of these infections and the course they take. For details the original should be consulted.

HALAWANI *et al.* (p. 89) show that in long standing intestinal schistosomiasis with liver changes and enlarged spleen, the cephalin flocculation test and the colloidal gold test are often positive.

IGNACIO BALDO *et al.* (p. 1077) have examined by X-ray the lungs of a number of children infected with *S. mansoni*. Changes were found in about half, but seem to have been somewhat indefinite. There was evidence of myocarditis, with enlargement of the heart in some.

WELLS and DAMON (p. 96) use a wetting agent (Triton VE) with the acid-ether centrifugation technique, for the examination of faeces for eggs of *S. mansoni*. By this means they found eggs in 105 of 500 specimens without the wetting agent only 84 gave positive results. OLIVER-GONZÁLEZ and HERNÁNDEZ MORALES (p. 830) describe their method of examination of faeces for eggs of *S. mansoni* by a sedimentation technique which enables them to distinguish microscopically between living and dead eggs by observing the movements of the flame cells. They have applied this to patients after treatment with anthelmintic or urea stibamine the simultaneous disappearance of living and dead eggs suggests that dead eggs are either laid dead or die in transit from the place where they are laid. Dead eggs found in faeces are not necessarily eggs which have been a long time in the mucosa.

HERNÁNDEZ MORALES *et al.* (p. 300) find rectal biopsy much more accurate for the diagnosis of *S. mansoni* infections than either concentration methods of stool examinations, or antigenic skin tests. WELLS (p. 599) has designed a rectal scraper which, although not so effective for the diagnosis of *S. mansoni* infection as the acid-ether concentration method, may be a useful complement.

CLEBERTSON *et al.* (p. 912) show that extracts of cercariae of *S. mansoni* and of two other worms (not parasite in man) possess a common antigen which can be used for skin tests in schistosomiasis and other trematode infections. PRATT and OLIVER-GONZÁLEZ (p. 826) show that antigens prepared from cercariae of *S. mansoni* do not lose potency for intradermal tests if stored at 8°C. for 12 months. GOLDSTEIN (p. 328) describes an antigen he prepared by extracting adult *S. bovis* in saline. He has used this as an intradermal test for intestinal schistosomiasis. It is apparently useful, but the series tested was very small.

LÓPEZ (p. 914) regards palpable thickening of the sigmoid colon as a useful diagnostic sign of *S. mansoni* infection.

HERNÁNDEZ MORALES *et al* (p 731) find tartar emetic more effective than Fouadin in the treatment of *S. mansoni* infections, provided that 1 per cent solution is given intravenously in doses of 5 cc to a total of at least 120 cc, the injections being given on alternate days. A second course may be necessary.

HERNÁNDEZ MORALES *et al* (p 218) have used Anthiomaline in the treatment of *S. mansoni* infections in Porto Rico. Given by intramuscular injection in doses of 3 cc (i.e. 10 mgm antimony) on alternate days, to a total dosage of 45-48 cc, it rarely produces serious toxic reactions, and appears to be quite effective against the infection.

For the refractory proctitis often left after treatment of intestinal schistosomiasis, RADNA (p 99) has used histidine injections with success.

BRANDT (p 667) has found that adult *S. mansoni* can be removed from the portal vein of heparinized rabbits more easily than from non-heparinized rabbits, and suggests that heparin can be given to mobilize the worms, followed by introduction of an anthelmintic into the portal vein at operation.

KUNTZ and STIREWALT (p 434) have tested DDT against cercariae of *S. mansoni*. Its cercaricidal power is so slight, even under laboratory conditions, that it is not an effective agent for control of schistosomiasis.

JONES and BRADY (p 217) show that a (model) diatomaceous silica water filter was effective in preventing the passage of cercariae of *S. mansoni* in the Philippine Islands.

*S. japonicum*—A long and comprehensive report of *S. japonicum* infection in the Philippine Islands has been written by BANG and his colleagues (p 435). They make the startling remark that it is possible for half the population to be infected and yet for the infection to be unrecognized by the local physicians. In their surveys they used a sedimentation technique for examination of faeces, and they claim that if this method [or presumably some other concentration method] is not used, a large proportion of infections will be overlooked. In hyperendemic areas 80 per cent of children have enlarged livers, and the liver index is a useful guide to the prevalence of the disease. In Leyte, buffaloes and young pigs, and elsewhere rats, have been found infected. The only known snail host in the Philippines is *Oncomelania quadrasi*. American troops were infected in the course of engineering work associated with water, or while swimming or washing. For experimental work, guinea-pigs were found most suitable, and in therapeutic tests the efficacy of tartar emetic, Fouadin and anthiomaline was confirmed. Applications of benzyl benzoate or dimethyl phthalate to the skin affords some protection, and certain clothing materials commonly used in the U.S. army prevent penetration by cercariae, especially if the garments have been treated with benzyl benzoate, dibutyl phthalate, or a mixture of these.

WRIGHT *et al* (p 832) report on surveys made for schistosomiasis on Mindanao, Philippine Islands. PESIGAN (p 1013) has found a focus of *S. japonicum* on Mindanao. *O. quadrasi* is present in canals and rice fields.

*S. japonicum* has been found in 11 districts of Szechwan, China, a province formerly regarded as relatively free. KUO (p 331) indicates that *Schistosomophora slateri* may be the snail host in some areas.

VOGEL (p 330) has crossed *S. japonicum* with *S. mansoni* and a few of the resulting eggs produced embryos which developed in snails. The offspring resemble the female parent, and it is not certain that the process of reproduction is not one of parthenogenesis or pseudogamy.

The snail host of *S. japonicum* in the Philippines is *Oncomelania quadrasi*. McMULLEN (p 917) shows that this snail is amphibious and operculated, that it lives under varied conditions in scattered colonies, and that the main foci in which these snails come into contact with man are rice plots which have been abandoned for a time. He has observed the growth of these snails, their life-span is at least one year and they may be infected shortly after hatching.

McMULLEN and GRAHAM (p. 917) think that under war conditions, impregnated clothing and protective ointments offer considerable protection against cercariae of *S. japonicum* but because no cercaricidal substance has yet been found effective in large bodies of water practical control entails elimination of the snail host (*O. quadrasi*). Chemicals are best used against this amphibious species in the dry season. The authors tested 19 chemicals on plots of ground—they were effective in killing the snails in different concentrations, but all except two dinitro compounds injured the vegetation. Drainage and removal of the taller vegetation are also needed for the best results.

McMULLEN and INGALLS (p. 917) tested 10 chemicals against cercariae of *S. japonicum*. These had also been used in tests against *O. quadrasi*. Details should be sought in the original.

INGALLS (p. 447) has studied the action of salt water on the cercariae of *S. japonicum*: sea water with 3 per cent. salt is lethal to cercariae within 3 minutes, but 1.5 per cent. is not, and such water is potentially dangerous to man, for instance where sea water is diluted by river water.

FAUST (p. 833) shows that eggs of *S. japonicum* (from the Philippines) may remain viable in the cold (at 4°C.) for 27 days if stored without washing and up to 6 months if stored after washing. Winter temperatures in China and Japan are too low for hatching.

FAUST and INGALLS (p. 331) discuss the various techniques that have been used for examination of faeces for eggs of *S. japonicum*. They make the point that the zinc sulphate centrifugal floatation method is not satisfactory because only a small proportion of the eggs will float. Direct smear is useful, but sedimentation after homogenization in 0.5 per cent. glycerin in water, either centrifugation, and the technique in which sodium sulphate solution, a detergent and ether are used, with centrifugation, produce better results. The subject is discussed in detail and readers should consult the original. HURTIS *et al* (p. 440) also write in favour of the last method.

BAROODY and MOST (p. 333) find that if faeces are diluted with water and centrifuged, several times, examination of the sediment for eggs of *S. japonicum* gives more positive results than direct smear and than the ether-zinc sulphate or brine floatation methods. This method has the additional advantage that it is simple.

HOLLANDS and PALMER (p. 429) have found that aspiration of the rectal crypts (even if normal in appearance) or scraping and aspiration of suspected lesions, is a valuable means of diagnosis of *S. japonicum* infection when faeces are negative. Aspiration is carried out with a motor-driven suction pump and a glass pipette which are described.

An antigen consisting of a saline extract of cercariae of *S. mansoni* is not species-specific (though it shows a high degree of specificity for trematodes) and HARTZ and MOST (p. 440) have used it with success in an intradermal test for the diagnosis of *S. japonicum* infections. The tests became negative within 8 months in many persons who received Fouadin treatment—they therefore have a value for prognosis.

WRIGHT *et al* (p. 833) prepared antigens from adult *S. mansoni* for use in intradermal and flocculation tests for *S. japonicum* infection. The intradermal test gave somewhat disappointing results, especially in early cases, and only 83.7 per cent. of 104 persons microscopically diagnosed gave positive results with the flocculation test. Some non-specific reactions were observed.

WILLIAMS (p. 399) shows that a complement-fixation test, with an antigen prepared from livers of *Planorbis eximius* heavily infected with *S. japonicum* is outstandingly effective for the diagnosis of *S. japonicum* infections. The test is more sensitive and less tedious than repeated examination of the stools for ova.



She quotes the results, in 560 men examined, on which she bases her conclusions. DAKIN and CONNELLAN (p 915) give an account of the outbreak referred to by Williams above, and report the same tests, but they also describe the symptoms, and the results of treatment with Fouadin, which were poor.

WINKENWERDER *et al* (p 834) report on 364 cases of *S japonicum* infection in United States troops in the Philippines. The incubation period was from 26 to 58 days, and ova were found about one month after the onset of symptoms. Eosinophilia, often to 85 per cent of the total leucocytes, was a common finding. Yellowish nodules were observed in the intestinal mucosa on sigmoidoscopic examination, and these were regarded as evidence of relapse after treatment. Fouadin, tartar emetic and anthiomaline were used in treatment, the relapse rate with Fouadin was about 40 per cent. MARTIN *et al* (p 334) note that a story of prolonged fever with urticaria, weakness, diarrhoea and other abdominal symptoms was the most significant clinical finding in American soldiers infected with *S japonicum*.

LEAVITT and BECK (p 916) make the point that *S japonicum* infection was asymptomatic in a considerable number of members of an American hospital staff in the Philippine Islands. Diagnosis was made by examination of faeces and the recognition of small lesions (stellate distended venules, sometimes with a central pustule or ulcer) in the recto-sigmoid mucosa. Eggs were found in scrapings from these lesions.

MASON *et al* (p 732) report on American soldiers admitted to hospital some 6 months after the onset of acute symptoms of schistosomiasis. Early symptoms included fever and abdominal pain, sometimes with diarrhoea and palpable liver, rarely with urticaria and palpable spleen. Eosinophilia over 9 per cent was common. Diagnosis during the later stage, by finding *S japonicum* in the faeces, was rarely positive at the first attempt, and sometimes needed 10 or more examinations. Lesions detectable on proctoscopy were very rare. Eight of 481 patients showed neurological symptoms and two who were accidentally killed showed military abscesses in the liver. Treatment with potassium antimony tartrate (0.5 per cent) gave better results than treatment with Fouadin.

TILLMAN (p 600) discusses cerebral involvement in *S japonicum* infection and reports 7 cases in which this diagnosis was made on clinical grounds. The symptoms are described, none of the patients (American soldiers) died, but treatment with antimony was only partly successful. WATSON *et al* (p 916) describe a case of cerebral involvement in *S japonicum* infection, lesions in the brain were recognized at operation, the patient having had convulsive seizures, and localizing signs being present. CUTLER (p 1079) also describes a case of *S japonicum* infection in which the central nervous system was involved, treatment with Fouadin was very beneficial and the author advocates it, as early as possible.

Two cases of acute pulmonary lesions due to *S japonicum* are described by WEINBERG and TILLINGHAST (p 441), the radiographic appearances suggested military tuberculosis due, in one fatal case, to pseudo-tubercles which had formed around schistosome eggs. Cough, pain and scattered râles were present.

LIPPINCOTT *et al* (p 601), having made tests of liver function in *S japonicum* infection, conclude that antimony treatment has a minor effect on the liver.

*Other trematodes*—BERTRAND (p 1080) reports a case of paragonimiasis from the Belgian Congo. FEDERICO HEINERT (p 1080) reports 26 cases of paragonimiasis from Ecaudor, discovered during the last 25 years. Most of the patients were cured by emetine.

DE OLIVEIRA and MEIRA (p. 668) diagnosed *Clonorchis sinensis* by examination of bile obtained by duodenal drainage in a man born in Shanghai, who lived in Brazil.

FRIESS (p. 442) describes three cases of infestation with *Fasciola hepatica* in one family in Algeria. Infection was probably acquired from watercress. Only one showed symptoms—loss of weight, slight fever, anorexia, anaemia and eosinophilia.

BOXNE *et al.* (p. 1013) describe a new echinostome parasite of man in Java, *Echinostoma reomanum*, and discuss the probable snail hosts.

In Oregon, MACFARLANE and MACY (p. 897) describe a new species of cercaria (*C. oregonensis*) which causes swimmers' itch. The host snail is *Physa ampulacea*. The authors observed that the cercariae seemed to penetrate the skin as the water containing them evaporated. The dermatitis lasted from 1 to 4 weeks.

### Cestodes

In a study of the life-cycle of *Diphyllibothrium mansonii* in Tonkin, GALLIARD and NGU (p. 733) have found that three intermediate hosts (instead of two) are apparently necessary. The cycle is dog-*Cyclops* tadpole-frog. Experiments to infect frogs by feeding them on infected *Cyclops* failed, but tadpoles could be so infected, and frogs could be infected by ingesting infected tadpoles. The authors therefore regard tadpoles as essential intermediate hosts.

A human case of sparganosis (undifferentiated) was reported, for the first time in the Belgian Congo, by FAIX (p. 1080).

Evidence is produced by von BONADONOFF (p. 1081) that pernicious tapeworm anaemia (*Diphyllibothrium latum*) is due to interference by the worm with the interaction between intrinsic and extrinsic factors. The site of this interaction is probably the intestinal wall.

DICKMAN (p. 221) describes four cases of cysticercosis of the posterior cranial fossa.

NEGEMME and FAIGUENBAUM (p. 734) have treated various forms of taeniasis with quinacrine apparently with success.

A method for biological estimation of substances used in treating cestode infestations is described by HOLTON (p. 835).

VAN AMERONGEN (p. 734) notes that *Echinococcus granulosus* infection is common in dogs in the Dutch province of Gelderland, especially on farms where slaughter regulations are lax.

DUXDAL (p. 100) discusses the great reduction which has been made in the incidence of human hydatid disease in Iceland, where it was once very common. The decrease is ascribed largely to education of the people and to anthelmintic treatment of dogs each year.

In Egypt, EL KORDY (p. 601) shows that hydatid disease is common in camels (31 per cent.), buffaloes (16), cattle (16) and sheep (1.5 per cent.).

COSK (p. 602) describes the Australasian Hydatid Register with 1,802 cases, almost equally from Australia and New Zealand. Most of the cysts were in the liver.

BRISOU (p. 222) has used, for the diagnosis of hydatid disease, extract of tapeworms of different species with which he performs intradermal tests. The active substance is a polysaccharide fraction joined to a distinct protein fraction, and it is about as specific as the antigen obtained from hydatid fluid. It is necessary to know if the patient has had tapeworm infestation previously. Details of preparation are given.

WATSON (p. 222) confirms a previous finding by STEWARD that *Hymanolepis muris* is found in Syrian hamsters but his investigations do not indicate that there is much danger of infestation of laboratory attendants who handle them.

HARANT *et al* (p 1013) found *Hymenolepis nana* in a child suffering from persistent diarrhoea, in Montpellier. Three other children in the same family were also found to be infected, and the authors report that almost half the population had suffered from persistent enterocolitis during the same summer. Infection had presumably been introduced by French African troops stationed there.

Charles Wilcocks

[To be continued]

## RABIES

JACOTOT, H. L'addition de latex d'*Hevea brasiliensis* au vaccin antirabique formolé en vue d'augmenter son activité [The Addition of the Latex of *Hevea brasiliensis* to Formolized Antirabio Vaccine as a means of increasing its Activity] *Ann Inst Pasteur* 1948, Jan, v 74, No 1, 53-4

The addition of a small amount of the latex of *Hevea brasiliensis* to antirabic vaccine prepared from formalized brain pulp increases appreciably the activity of the vaccine. Results of experiments described indicate that only 9 of 57 guinea-pigs which received the vaccine containing the latex succumbed to the virulence test, compared with 34 out of 57 which received the vaccine without latex. In other words 84 per cent of the first group, but only 40 per cent of the second were protected. All of 19 non-vaccinated control guinea-pigs died.

These results are similar to those obtained when alumina gel was used as an adjuvant [see this *Bulletin*, 1948, v 45, 291] H J O'D Burke-Gaffney

EMLINGER, P & BAILLY, J. L'extension des vaccins antirabiques phéniques et la nécessité d'une Conférence internationale de la rage [The Increasing Use of Phenolized Vaccines in Anti-Rabies Treatment and the Need for an International Conference on Rabies] *Bull Acad Nat Méd* 1948, v 132, Nos 9/10, 166-8

In this paper communicated to the National Academy of Medicine in Paris at its meeting on 9th March, 1948, the authors again advance arguments in favour of the general adoption of phenolized killed virus vaccine for use in anti-rabies treatment.

Moreover they make a strong plea, based on the experience of French North African territories and elsewhere, not only for canine prophylaxis but also for the curative treatment of dogs and other domestic animals bitten by rabid animals.

In this connexion surprise is expressed that, by failure to recognize the greater utilitarian value of phenolized vaccines and the need for the vaccination of animals other than man, France has not kept abreast with modern ideas on anti-rabies treatment.

With a view, therefore, to having the whole subject of anti-rabies treatment reviewed and, if possible, uniformity of procedure reached, the authors urge the early calling of an international rabies conference, similar to that held in Paris in 1927. Items on the suggested agenda include the nature of rabies virus, its culture, the influence of passage on the susceptibility of fixed virus to the action of attenuating agents, "rage de laboratoire" and paralytic accidents, rabies in the wolf and the intensive treatment necessary in the case of wolf bites, "failures" of treatment, criticism, particularly from the United States, of anti-rabies vaccination.

[The paper under review recapitulates the views expressed on anti-rabies treatment by the authors in their recent handbook *La Rage*—see this *Bulletin* 1948 v 45 387]  
G. Stuart

## MALARIA

SAUTET J. A propos de la régression spontanée "du paludisme. ["Spontaneous" Regression of Malaria.] *Bull. Soc. Path. Exot.* 1948, v 41 Nos. 1/2, 31-3.

As a result of observations in Corsica, the author in 1933 put forward the hypothesis that the so-called "spontaneous" epidemiological regression of malaria might be due to a limited tendency for the parasite concerned to form gametocytes, so that mosquitoes had less chance of becoming infected.

He now refers to an epidemic of malaria in Camargue in 1943 where endemicity of malaria is normally very low. In this outbreak, he was struck by the absence of gametocytes in the blood of those infected with the strain of *P. vivax*. This epidemic soon waned, giving place to the previously low endemicity.

These results contrasted strikingly with those found in intensely malarious areas in Corsica, where he had noted a gametocyte index of 26.3 per cent. or in the Lebanon where an index of 20 per cent. was found among Armenian refugees.

He refers to the results of SERGEEV and TIBURSHAYA [this *Bulletin* 1945 v 42, 622] who found that a strain of *P. vivax* from a southern region of the U.S.S.R. showed a greater tendency to produce gametocytes than did a strain from a northern region.

The author concludes that these findings support his thesis that the epidemiological regression of malaria is largely due to the limited capacity of the responsible strain to produce gametocytes. H. J. O. D. Burks-Gaffney

DORLEMAN H. & VAN TRIJK, P. H. De malaria-epidemie te Middelburg in de jaren 1940 tot en met 1945 benevens een onderzoek van parasieten dragers. [The Malaria Epidemic at Middelburg 1940-1945 and Parasite-Carriers.] *Nederl. Tijdschr. v. Geneesk.* 1948, May 1 v 92 (ii) No. 18, 131-138. English summary (9 lines)

The report on this epidemic was given in full by DORLEMAN [this *Bulletin*, 1948, v 43, 875] as a doctorate thesis. He concentrated attention on the parasite carrier especially the healthy carrier who makes little complaint of sickness, has a normal blood count and differential count and no alteration of his sedimentation rate. A few carriers showed lymphocytosis but there was no indication of monocyte increase. These parasite-carriers were treated and 65 of them were very strictly under observation for at least a year. None of them had a relapse either in the year or in the following year showing that they still had the advantage of premunition. Confirmation was obtained of the assertion that the variation in the number of parasites was periodic: 10 to 16 days of a positive phase and 8 to 14 days of a negative phase. This was an important observation for the control of a parasite carrier. It was not necessary to examine the blood daily but only 10 days and 16 days respectively after the previous examination.

That epidemic malaria occurred in Middelburg and nowhere else in Zeeland is explainable by (1) the presence of parasite carriers (2) the incursion of parasite carriers and (3) conditions satisfactory for the maintenance of anophelines. The first of these explanations is the same as to state that

malaria is endemic in Middleburg the second refers to the occupation of barracks by Germans, and the third to the presence of military horses in the centre of the town, so that more anophelines were attracted there than in normal years

Now that Zeeland and Walcheren have been freed of malaria, responsibility that they shall continue to be free belongs to the medical practitioner. He should report all cases of malaria, see that blood examinations are carried out and go carefully into the question whether the case is autochthonous

W. F. Harey

GARACI, C. L'andamento dell'infezione estivo-autunnale in Cassino [The Course of *P. falciparum* Infections in Cassino] *Riv di Malariaologia* 1947, Dec., v 26, No 6, 283-95, 4 charts [16 refs.] English summary

The communes in the neighbourhood of Cassino were not malarious before the war, but after the destruction wrought by war in 1943 malaria became both prevalent and severe. The disease was widespread in 1944. *P. vivax* infections were most in evidence and only a few *P. falciparum* infections were identified. In the following year, however, *P. falciparum* became widely diffused and there were many fatalities. In July 1945, the Rome Institute of Malariaology opened a diagnostic centre in Cassino and the results of some of their investigations are summarized in this report.

During the last six months of 1945, 2 312 blood samples were examined of which 58 per cent were positive for malaria. Of positive findings, 60.5 per cent were *P. vivax* and 39.5 per cent *P. falciparum*. In 1946, of 3,124 bloods examined, 66 per cent were positive, *P. vivax* 86.1 per cent, *P. falciparum* 13.9 per cent.

*P. falciparum* infections rose in July and increases followed in August and September. The decline in the incidence curve commenced in October. In Central and South Italy, as a rule, the *P. falciparum* incidence curve rises steeply in July and August and thereafter declines almost as steeply. The July rise is hard to explain. In June, gametocyte carriers were very few, the mean temperature was only about 21°C, at which temperature the extrinsic cycle of development of *P. falciparum* is of about a month's duration. It is hardly likely that the early cases were relapses of infections contracted in the previous year.

Norman White

HEISCH, R. B. A Parasitological Survey of Taveta. *East African Med J* 1948, Feb., v 25, No 2, 78-94, 5 figs

This paper is a continuation of the author's parasitological surveys in Kenya Colony [this *Bulletin*, 1947, v 44, 678] and refers to conditions in the small Taveta reserve, close to Kilimanjaro. Future workers will undoubtedly find these records of great value, surveys in new countries today are so often handicapped by having no historical background. Also, a widespread sampling of the population and its environment is always likely to reveal something of immediate interest, and here the author has discovered a condition of splenomegaly which cannot be ascribed to any of the ordinary causes. The spleen rate of one group of adults living near Lake Jipe was 58 per cent while the malaria parasite rate was only 18 per cent, a peculiar relationship for inhabitants exposed to hyperendemic malaria, where both rates should be low. This group showed, in addition, an 11 per cent infection rate with the ova of *Schistosoma mansoni* on single stool examinations and it is suggested that the high adult spleen rate may be due partly to the presence of this helminth.

*Miss.*, and *sicantii* Roub. and *A. sackarovi* Favr. The geographical distribution of the three species is shown on a map, and a new specific group within the subgenus *Anopheles* named *Mical perusa* is erected for them. The diagnostic characters of this group are described, and characters are given in a table distinguishing the three species in the egg, larval and adult stages (these last consisting mainly of differences in the male hypopygia) with notes on habits. A list of the Italian Anophelinae is included.

YOCKO M. D., HARDMAN N. F., BURGESS, R. W., FROMYER W. C. & SABROSKY C. W. The Infectivity of Native Malaria in South Carolina to *Anopheles quadrimaculatus*. *Amer J Trop Med.* 1948, Mar., v 28, No. 2, 303-11 1 fig.

The susceptibility of anopheline mosquitoes to infection with the different species of malaria parasites has usually been worked out in the laboratory by means of artificial infections. In this investigation, natural infections were used and their infectiveness to the local anophelines (*A. quadrimaculatus*) was determined. The patients were negroes living in South Carolina and were known to have had malaria within recent months. A hundred mosquitoes were fed on each patient irrespective of whether his blood contained gametocytes or not or even parasites of any sort. 14,811 mosquitoes were fed in 165 lots. 142 lots were fed upon *P. falciparum* patients. 14 lots on *P. malariae* and 9 on *P. vivax*. The last were all negative (in fact at the time of feeding, only one case showed parasites and these were all asexual). The *P. malariae* cases showed gametocytes in four instances and three of them infected the mosquitoes. Twenty five patients out of the 14 *P. falciparum* cases showed gametocytes, all in low density and 16 of these infected mosquitoes. Some of the patients showed neither sexual nor asexual parasites at the time of feeding, and yet four of these cases were infective to mosquitoes. The patients without symptoms were just as efficient carriers as those with symptoms. The whole trend of these experiments shows that gametocyte density can be extremely low and yet mosquitoes can become infected under such conditions. The majority of the infections resulted from feeds on people showing fewer than 10 crescents per cmm. of blood. One patient with a *P. falciparum* infection was able to infect mosquitoes throughout a period of eight months. The duration of this species of infection appeared to approach a year but further work is progressing to determine the exact duration. P. C. C. Garnham

WILLIS, E. R. The Olfactory Responses of Female Mosquitoes. *J. Econom. Entom.* 1947 Dec., v 40 No. 6, 769-78, 2 figs. [13 refs.]

*Anopheles quadrimaculatus* and *Aedes aegypti* were used in a series of experiments in an attempt to observe and record their olfactory responses. Most of this paper consists of a description of the olfactometer and the experimental technique and is not easily summarised.

A diagram is given of the apparatus through which two streams of air are passed, either could carry an odour while the other served as a control. Light, temperature, humidity and other factors are regulated.

For each test, 50 female mosquitoes of known age were placed in a wire cage with a glass front, into which the two air streams arrived. Photographic records were made of the mosquitoes' movements at intervals of one minute for a test period of ten minutes. Counts were made on the developed films, which showed the numbers and distribution of the insects.

Data are presented which show that non-blood-fed females of both species were attracted by the odour of the human arm when the air was at 34°C and

between 70 and 85 per cent relative humidity. Blood-fed females of *Aedes aegypti* and males are not attracted to arm odour. There was no indication that carbon dioxide in 1, 10 or 50 per cent concentrations was attractive to either species [See also this *Bulletin* 1947, v 44, 787].  
H S Leeson

ROSENSTIEL, R G. Dispersion and Feeding Habits of *Anopheles freeborni*. *J Econom Entom* 1947, Dec, v 40, No 6, 795-800, 3 figs [13 refs]

One method of studying anopheline dispersion from breeding places is by marking, releasing and recovering female mosquitoes. Another is by measuring population fluctuations at successive distances from the breeding places. The latter method (adopted by the author) can only be used where breeding places are isolated. Two such breeding places were found in the Sacramento Valley. One is referred to in this paper as the Dixon-Suisun area and the other as the Yuba City area.

The adult haunts chosen for study were those where *Anopheles freeborni* had been found the previous year. They were barns, basements, sheds, bridges and culverts which were situated at varying distances from the breeding places at intervals of a mile or two. They were visited once a week when mosquitoes were collected, counted and examined for eggs, fat body and species, then carefully returned alive to their resting places.

The two areas were divided into zones and the data recorded on charts. From these it is observed that no dispersal occurred until mid-July. Then there was a congregation of adults around the breeding places which went on until some time in the last three weeks in August, during which time the females were feeding. The numbers then declined about the breeding places and increased in the resting places up to five miles away where there were no areas for breeding. During September and October dispersal was very active and was most noticeable within ten miles of the breeding places.

Adults from the Yuba area were found at least 4-5 miles to the south and some from the Dixon-Suisun area travelled at least 26 miles. Feeding went on during the dispersal and females contained eggs, hibernating ones contained fat and those which managed to survive the winter were seen to contain eggs, fat or blood in the following February.

SILVA, W. Contribuição ao estudo da história da malária na cidade do Salvador—Bahia [A Contribution to the Study of the History of Malaria in the City of Salvador, Bahia]. *Rev Med-Cirurg Brasil* 1945, v 53, Nos 2/3, 17-59, 5 graphs & 1 diagram [56 refs] [Summary taken from *Rev Applied Entom* Ser B 1948 Mar, v 36, Pt 3, 51-2].  
H S Leeson

The author outlines the history and geography of Salvador the capital of the State of Bahia, Brazil, in which malaria has been endemic and occasionally epidemic, since it was first built. In 1929, *Anopheles argyritarsis*, R-D, *A. albiparvus*, Arrib, and *A. aquasalis*, Curry (*tarsimaculatus*, auct.) were found to be common in the city. In 1936 a malarial service was instituted, the work of which included the inspection of dwelling-houses, the collection and identification of mosquito larvae and adults, and the preparation of blood smears. Tables and graphs are given showing data obtained in 1937-41 on the incidence of *Plasmodium falciparum* and *P. vivax* in persons of different age-groups, and on the distribution of Anopheline breeding places. The larvae most commonly found were those of *A. aquasalis*, *A. argyritarsis*, *A. albiparvus*, *Aedes scapularis*, Rond, and *Anopheles triannulatus*, Neiva & Pinto (*bachmanni*, Petrocchi), in that order. Adults of the first three species and of other

density. In uninfected children, the percentage is 2-4, in those with a low density it rises to 3-6 and in those heavily parasitized it may be over 12. The author concludes that persistent sub-clinical infections in African children are accompanied by increased erythropoiesis, the increase being related to the density of the infections.

P. C. C. Garaskin

CICCONARDI A. & ALFANO A. Sul reticolocitotropismo del plasmodi nella malaria. Nota I.—Il diametro medio delle emazie mature e dei reticolociti durante l'accesso tertanario da *Plasmodium vivax*. [Reticulocytotropism of *Plasmodium*. V. Diameter of Mature Erythrocytes and of Reticulocytes during *P. vivax* Infection.] *Atti Med. Italiana*, 1948, Jan., v. 3 No. 1 13-17. English summary

The authors have studied the blood cells during attacks of *P. vivax* infection. As regards uninfected cells it is possible to identify macro-erythrocytes and macro-reticulocytes. Infected cells gave an average diameter which is greater than that of uninfected cells. The average diameter of infected red cells is very near that of infected reticulocytes.

C. M. Wexon

ANDREWS W. H. H. & MARGRATH B. G. The Pathogenesis of the Liver Lesion due to the Administration of Carbon Tetrachloride. *Aust. Trop. Med. & Parasit.* 1948, Apr., v. 42, No. 1 85-100 8 figs. on 2 pls. [30 refs.]

The effect on the liver of carbon tetrachloride, chloroform, and phenylhydrazine has been investigated in the course of experiments designed to elucidate the pathogenesis of the centrilobular changes found in malaria. Most of the experiments were made on rats, but other animals were also used. All the drugs produce central necrosis of the liver. The pathological changes are well-known, and are described briefly. In most species the necrosis was accompanied by swelling of the parenchymal cells in the mid-zone causing narrowing of the sinusoids. These vascular changes were investigated in greater detail by injection of Indian ink into the splanchnic system. In animals which had received carbon tetrachloride the penetration of Indian ink into the liver lobules was much reduced.

In the discussion it is pointed out that poisons which cause central necrosis of the liver cannot do so by a direct action on the liver cells, for in that case the cells most affected should be those first reached by the drug at the periphery of the lobule. It is suggested that the necrosis is produced indirectly—swelling of the parenchymal cells obstructs the blood flow to the centre of the lobule and the resultant anoxia leads to necrosis. It is not clear whether this swelling is a direct effect of the poison or whether it also is a result of anoxia, caused by a reflex constriction of the blood vessels. There may be other mechanisms causing central necrosis, since in some cases congestion and not constriction of the sinusoids is found after giving carbon tetrachloride.

[This paper should be read in conjunction with that of GLENN and HUSKOWITZ (*Clinical Science* 1948, v. 6, 235) who injected Indian ink into the spleen of rats at varying intervals after a dose of carbon tetrachloride. They found the same impairment of penetration of the ink into the centrilobular sinusoids, and drew the same conclusions. These authors pointed out that both carbon tetrachloride and ligation of the blood vessels to the liver produce central necrosis, and in both cases there is a time-lag of 4-8 hours before the necrosis is fully developed. This is further evidence of a common factor in the two processes, which may be anoxia. They also observed that necrosis may occur in other conditions in which the liver cells are swollen—e.g. when they are loaded with fat.



Studies of this kind are clearly relevant to any discussion of the relation between interstitial tissue and parenchyma.] *J C Waterlow*

SCHNEIDER, T **Haematemesis in Malaria** *South African Med J* 1948, Apr 24, v 22, No 8, 289-91

This report concerns an African male of about 38 who was admitted to hospital in Johannesburg in May 1946 with headache and dizziness which had been present for a week, during which he had had one attack of unconsciousness and one attack of haematemesis. He had no history of gastric symptoms, he had visited a malarial area the month before, but had no personal history of malaria.

On admission the patient had a temperature of 102.4°F and looked ill, but examination revealed little of note, except the examination of the blood. This showed the haemoglobin to be 20 per cent, and the erythrocytes 1,140,000 per cmm. No malaria parasites were found. Despite daily slow transfusions of citrated blood, haematemesis and melaena occurred, the former being severe and persistent and being a daily feature. Hiccough appeared and became almost constant and the patient's condition was deteriorating. Ten days after admission, the erythrocytes were 1,430,000 per cmm and the haemoglobin 24 per cent, and the anaemia was reflected in the blood picture. On this occasion, however, many *P falciparum* parasites were found in the blood. Quinine bisulphate was given (10 grains, t.d.) and haematemesis stopped within 24 hours. Quinine was continued, the temperature fell to normal, and the haematemesis, melaena and hiccough disappeared. After a course of mepacrine, the patient made a good recovery and left hospital seven weeks after admission. An X-ray examination revealed no sign of gastric or duodenal ulceration.

A feature of the case was that the prothrombin index, bleeding time and clotting time were normal. The author compares this with other cases in the literature. The cause of the haematemesis is discussed and the author concludes that the condition was due to a toxic process leading to gastrostaxis initiated by the malarial parasite, since other causes would not be expected to result in so dramatic a response to quinine. Malaria should be considered as a possibility in cases of haematemesis coming from malarial areas.

*H J O'D Burke-Gaffney*

PARAF J & LEWI, S Réactions sérologiques faussement positives chez un paludéen anémique et ancien syphilitique [False Positive Serological Reactions in a Case of Malaria with a History of Syphilis] *Bull et Mém Soc Méd Hôp de Paris* 1948 Nos 12/13, 412-14

Report of a case

COATNEY, G R, COOPER, W C & RUHE, D S **Studies in Human Malaria. VI The Organization of a Program for testing Potential Antimalarial Drugs in Prisoner Volunteers** *Amer J Hyg* 1948, Jan, v 47, No 1, 113-19, 1 fig

In studies designed to test the comparative efficacy of drugs, old and new, in the treatment of malaria, an important contribution was made by white volunteer prisoners in the United States Penitentiary, Atlanta, Ga, who willingly underwent the discomforts and uncertainties both of malaria and of the experimental drugs. This paper describes the organization of these studies. One hundred and twenty volunteers were infected with malaria by the bites of infected *A quadrimaculatus*. The St Elizabeth strain of *P vivax* was used to infect 105. The remainder were infected with the Chesson strain which

originated in New Guinea. The complete testing of a drug included a long term protective test, a short term protective test, and therapy during acute attacks of malaria. Observations were made on toxicity and quantitative estimations of drug in plasma or whole blood were carried out. Observation of patients continued for 18 months after exposure to infection. *Norman White*

COATNEY G. R., COOPER, W. C., ROME D. S., JOSEPHSON E. S., YOUNG M. D. & BURGESS R. W. Studies in Human Malaria. VII. The Protective and Therapeutic Action of Quinine Sulfate against St. Elizabeth Strain Vivax Malaria. *Amer J Hyg* 1948, Jan. v 47 No. 1 120-34 8 figs.

In the studies referred to above quinine sulphate was the first drug used. It was considered to be the logical standard of reference. Thirty volunteers were used in the protective tests. Each was exposed to the bites of 10 infected *A. quadrimaculatus*.

Quinine sulphate 0.5 gm. daily for four days before infection, on the day of infection, and for 20 days thereafter suppressed the early primary attack in all cases. Primary attacks occurred after prolonged latent periods of 270 to 332 days. A dose of 0.25 gm. a day for the same period failed to suppress the early primary attack in four of five individuals.

Doses of 2.0 or of 0.5 gm. daily from the fourth day before to the sixth day after infection failed to suppress the early primary attack.

In the treatment of the acute attack doses of 2.0, 1.0 and 0.5 gm. daily for 8 days were used. Parasites disappeared and fever was controlled in all cases, the rate of action being roughly proportional to the dose used. Relapses occurred after intervals that were not influenced by the dose of quinine given in the treatment of the previous attack.

Toxic symptoms were frequent and at times severe: stimulus, partial deafness, blurring of vision, nausea and vomiting and urticaria, in that order of frequency were noted. *Norman White*

YOUNG M. D. & EYLES, D. E. The Efficacy of Chloroquine, Quinacrine, Quinine and Totaquine in the Treatment of *Plasmodium malariae* Infections (Quartan Malaria). *Amer J Trop Med* 1948, Jan. v 28, No. 1 23-8, 3 figs.

Fifty-four neurosyphilitic patients both white and negro were infected by the injection of blood containing *P. malariae*. When treatment started, 41 of these patients had experienced 15 or more febrile paroxysms. In some the infections had recently become asymptomatic but parasites persisted in the peripheral blood. The dosage of the drugs used was —

Chloroquine 0.6 gm. followed 6-8 hours later by 0.3 gm. 2nd and 3rd days, 0.3 gm. in single dose each day. In some cases the single daily 0.3 gm. doses were continued to and including the 6th day.

Quinacrine (mepacrine) 0.1 gm. thrice daily for 5 days, or three days the first day 1.0-1.0-0.3 and 0.3 gm., followed by 0.1 gm. thrice daily for 6 days.

Quinine 0.67 gm. thrice daily for 4 days then 0.67 gm. daily for several weeks.

Totaquine 0.67 gm. thrice daily for 14 days.

A comparison was made of the rates of elimination of parasites under each of these treatments. Chloroquine gave the best results. Quinacrine was more effective than quinine. Totaquine gave the poorest results. *P. malariae* responded relatively slowly to all the drugs tested. Chloroquine eliminates *P. malariae* parasites much faster than *P. malariae* parasites from the blood even when the densities of *P. malariae* parasites are several times higher. There was

no evidence that increased amounts of acquired immunity accelerate the action of antimalarial drugs in clearing the blood stream from parasites

Norman White

JAILER J W, ZUBROD, C G, ROSENFELD, M & SHANNON, J A Effect of Acidosis and Anoxia on the Concentration of Quinacrine and Chloroquine in Blood *J. Pharm & Exper Therap* 1948, Mar, v 92, No 3, 345-51 [13 refs]

SHANNON *et al* [this *Bulletin*, 1945, v 42, 343] drew attention to the great variations in plasma levels of quinacrine (atebrin) in individuals on the same dosage schedule. Recently the same authors [this *Bulletin*, 1948, v 45, 575] have indicated the effect on excretion of this and other drugs caused by oral administration of acid and alkali. The concentration of quinacrine in the tissues of animals was shown by MARSHALL & DEARBORN [this *Bulletin*, 1947, v 44, 292] to be more constant than in plasma and there was a greater correlation with intake as well as with suppressive effect on avian malaria. In the present investigation, the acid-base balance of blood and its degree of oxygenation were evaluated as factors likely to influence the partition of quinacrine and chloroquine (a 4-amino-quinoline) between plasma and tissues. The drugs were administered daily to dogs in aqueous solution by stomach tube for periods of from 2 to 18 days and treatment ended 24 hours before experiment. Ten dogs received quinacrine and two chloroquine. During experiment the animal, suitably anaesthetized, was allowed to breathe air for a period followed by 10 per cent  $\text{CO}_2$  in oxygen to produce acidosis. Anoxia was achieved, after a period of normal breathing, by means of lowered oxygen tension as a result of re-breathing air from which  $\text{CO}_2$  was absorbed. Gas analysis and pH measurements as well as estimation of drug levels were made on arterial blood the last named by the method of BRODIE & UDENFRIEND [this *Bulletin*, 1944, v 41, 453].  $\text{CO}_2$  caused a doubling of the drug concentration in plasma and in red cells but no appreciable change in that of muscle or leucocytes. There was a return to normal during the recovery period when air was breathed. The blood during acidosis was fully oxygenated, but the pH dropped to 6.9 and  $\text{CO}_2$  content rose steeply. Anoxia, on the other hand, caused no change in the drug concentration of red cells and plasma of dogs provided that the blood remained unaltered. The distribution of both drugs was high in tissue relative to plasma, and acidosis exerts its effect by altering the partition between the two. A considerable rise of concentration in the latter lowered only slightly that of the former. It appeared probable that the relative concentration of undissociated base is responsible for the distribution of drug between plasma and tissues.

J D Fulton

LAWANI, A, BAZ I & MORKOS, F On the Antimalarial Activity of Nivaquine C *J Roy Egyptian Med Ass* 1947, Dec, v 30, No 12, 665-9

Nivaquine C is 3-methyl-4 (diethylamino-pentyl) amino 7-chloroquinoline hydrochloride. The powder is very soluble in water and absolute alcohol. Tablets of the drug contain 0.1 gm. Nivaquine C is active against *P. praecox* in canaries and it is stated that in human malaria it is schizonticidal, but has a weaker action on gametocytes. The authors quote DECOURT and SCHNEIDER [see this *Bulletin*, 1948, v 45, 148] in Tunis as having treated adults with 0.3 gm for 5 days without any relapses after a year but "the number of cases was not sufficient to allow of definite conclusions to be drawn".

The present authors investigated the antimalarial activity of Nivaquine C on 98 ambulatory patients at Khanka near Cairo. The patients were put on the following schedule —

First day	3 tablets in the morning 2 tablets in the evening
Second day	2 tablets in the morning 2 tablets in the evening
Third day	2 tablets in the morning 1 tablet in the evening

Fourth and fifth day the same dosage as on the third day

All infections were due to *P. vivax* except one which was a *P. falciparum* infection, in which rings and crescents were present. This patient did not complete the treatment.

In 48 cases pyrexia and parasites disappeared after the first day of treatment. The remainder responded after 2 days. Gametocytes required a few days more.

No toxic symptoms were observed. Only 9 patients relapsed, and a table compares these with the monthly incidence of malaria in the various villages concerned for three to five months. This average was about 1% per cent, compared with an average of 9.3 per cent. of relapses among 93 cases treated and followed up during the same period. It would appear that the incidence of malaria among those treated with Nivaquine was less than that in the general population of the villages in which they resided.

It is concluded that Nivaquine is a potent antimalarial drug, which does not produce toxic effects in the doses suggested. It is mainly schizontocidal and gametocytes take a longer time than asexual forms to disappear after its use.

H. J. O. D. Burke-Gaffney

SHUMLER, H. O. MILLMAN, N. & BOSWORTH, Mary R. Toxicity and Pharmacology of SN 13592. An Analogue of Phenyl Panthothenone. *Proc. Soc. Exper. Biol. & Med.* 1948, Mar. v. 67 No. 3 384-86 700.

SN 1359<sup>2</sup> is characterized by an extremely low acute and chronic oral toxicity in several species. Local irritation effects are absent even upon repeated administration. Continued oral feeding of the drug, induces an anemia which gradually disappears after the drug is withdrawn. Although there were no consistent effects on blood pressure and heart rate a respiratory effect was noted. Smooth muscle was generally stimulated by this compound.

MURCHMATER, J. H. TENICK, F. H. JONES, E. M. JONES, FARRAR, A. HOLLOWAY, W. F. & RAWLIN, A. L. Amodiaquiphensols as Antimalarials. II. (Heterocyclic-amino)- $\alpha$ -amino- $\alpha$ -cresols. The Synthesis of Camoquin. *J. Amer. Chem. Soc.* 1948, Apr. 70 No. 4 1263-73

LUTE, R. F. & ROWLETT, M. J. J. Antimalarials. 2,2-Diphenyl-3-(aryl) Amino Ketones and Alcohols. *J. Amer. Chem. Soc.* 1948 Apr. 70 No. 4 1332-43

YUST, H. R. DDT to control *Anopheles farauti* on Espiritu Santo, New Hebrides Islands. *J. Econom. Entom.* 1947 Dec. 40 No. 6, 62-8, 1 fig.

Among the troops on Espiritu Santo and adjacent islands, there were over 400 primary malaria infections in January 1943 and the same number in February. *An. Pulex farauti* is the only anopheline on these islands and all stages are present all seasons. An attack on this mosquito by the usual methods of control was started and by December 1943 primary infections were

down to 41 for the month for March 1944 the figure was 19. In April of that year DDT became available. Preliminary investigations showed that 10-minute catches in huts by two men averaged 73 *A. farauti* per hut. The DDT was first tested in cages and in the huts and then in July 1944 every hut and building was sprayed with 5 per cent DDT in kerosene at the rate of 1 gallon per 1,000 square feet of surface, by means of a knapsack sprayer. In some cases, 10 per cent DDT water suspension was applied by flit gun. This treatment was later extended to native huts and plantation buildings. Larval control by weekly spraying of breeding places with 2 quarts or more per acre of 5 per cent DDT in kerosene was done by hand sprayers, knapsack sprayers and by aeroplane. No adult *A. farauti* was found during the rest of the year, and while in May, 1 456 larvae had been found in 38,701 dips, in October only 20 larvae were obtained in 42,525 dips. The average military strength during 1944 was just over 40,000 troops, but there were no primary malaria infections during November and December.

GALVÃO, A. L. A. & DAMASCENO, R. G. Alguns dados experimentais sobre ação do DDT e do piretro contra o *Anopheles darlingi*. [Experimental Study of DDT and Pyrethrum as Active Agents against *Anopheles darlingi*. Rev. Serviço Especial de Saúde Pública. Rio de Janeiro 1947, July, v. 1, No. 2, 273-92, 3 figs & 5 graphs. [11 refs.] English summary. H. S. Leeson

"1 The *A. darlingi* mortality in a wood house treated with DDT dissolved in kerosene to give a final surface concentration of 2.09 gm. per square meter (195 mgr. per square foot) was determined. The mortality determined eight hours after contact was as follows: —One month post treatment 97.3 per cent, 2 months 96.4 per cent, 3 months 92.1 per cent, 4 months 95.3 per cent, 5 months 72.9 per cent, 6 months 67.7 per cent, 7 months 42.2 per cent. In the same period mortality observed in a control house was respectively, in per cent 4.4, 3.9, 3.3, 10.4, 3.7, 4.5, 6.3.

"2 The authors conclude that in houses of wood residual film DDT may be applied at intervals of 4 months in climates in which there is no interruption in *A. darlingi* breeding or perhaps two times a year where winter interrupts breeding.

3 Captures in houses treated with DDT done with windows open and with windows shut showed no appreciable difference from the point of view of prophylaxis. This causes one to predict that this insecticide will be equally effective in the unprotected dwellings of our people in general.

4 The killing of adult mosquitoes with pyrethrum spray reduced their numbers very much on the nights on which it was applied but apparently this reduction did not reach a point where the transmission of malaria would be prevented.

5 The action of pyrethrum was not lasting with respect to *A. darlingi* since there was no considerable diminution in density on the nights subsequent to the spraying.

GARNHAM, P. C. C. The Developmental Cycle of *Hepatocystes* (*Plasmodium kochi*) in the Monkey Host. Trans. Roy. Soc. Trop. Med. & Hyg. 1948, Mar., v. 41, No. 5, 601-16, 12 figs (7 coloured) on 4 pls. [15 refs.]

In a preliminary paper [this Bulletin, 1947, v. 44, 882] the author gave a short account of the exoerythrocytic schizogony of *Plasmodium kochi* in the liver of monkeys. In the present paper he gives a more complete account of the developmental cycle of this parasite, which he designates *Hepatocystes* (233)

*P. kochi* adopting the name proposed by LIXADITI and SCHÖN in 1932 for the schizont stage in the liver of the baboon, which they did not connect with *P. kochi*. The blood forms of the parasite are all gametocytes, the youngest stage being a minute spot of chromatin with a tongue of cytoplasm in a red blood corpuscle. With growth a large amoeboid ring is formed. The cytoplasm then becomes irregular in shape, and finally by a filling-in process, the spherical gametocyte is produced. The development of the gametocyte occupies 4 or 5 days. The mature gametocytes stain poorly in blood films. With Romanowsky stain the macrogametocyte takes a steely blue colour while the less dense microgametocyte stains a biscuit colour. The pigment is in the form of very fine granules and at no stage does the red blood corpuscle show Schüffner's dots. The nucleus of the male gametocyte is a large, oval-shaped pale pink area occupying a third to a half of the parasite. Scattered in the area are numerous deep red granules or threads of chromatin. The nucleus of the female gametocyte is much smaller and consists of a pale pink area with a dense mass of chromatin at the centre. Sometimes the single chromatin mass may be divided in two to six masses. The mature gametocytes appear to be extracellular and slightly larger than the normal red blood corpuscles. Attempts to infect clean monkeys by blood inoculation failed, though, transfer of gametocytes which appeared at once or later and persisted for periods up to 3 weeks took place. Exflagellation of the male gametocytes was easily observed. The infection in the monkey is very persistent and it is supposed that some of the merozoites from the liver schizonts must be asexual in character and able to give rise to fresh schizonts in the liver. The infected animals were not inconvenienced by their infection and showed no variations of temperature from the normal.

The schizogony in the liver has been described in the earlier paper. When a schizont is mature, merozoites are formed and these are scattered amongst the surrounding liver cells. They presumably find their way into red blood corpuscles to give rise to young gametocytes or into parenchyma cells of the liver to develop into schizonts. A liver cell is figured showing two undeveloped merozoites and two larger forms  $\frac{1}{2}$  and  $\frac{3}{4}$  in diameter. In the section, each of these has peripheral nuclei. A similar but larger form  $1\frac{1}{2}$  in diameter is figured. As the parasite grows, the infected liver cell hypertrophies, the parasite becomes irregular in shape and vacuolated while the nuclei multiply. Eventually the parasite assumes the form of a sponge with external protuberances and internal vacuoles. Finally the internal vacuoles coalesce leaving an external band of cytoplasm with irregular processes extending among the liver cells, and a large central vacuole. The cytoplasm is filled with nuclei which eventually form the nuclei of the merozoites. In fixed tissues cut for sections, the cytoplasm in the mature cyst tends to shrink from the surrounding liver cells, appearing as a band of cytoplasm enclosing the large vacuole. When smears of the contents of a cyst are made, the cytoplasm breaks into fragments of various sizes and with Romanowsky stain they take a blue tint with red nuclei. In the early paper these were described as cytomeres but it appears from sections that no definite cytomeres are formed. The mature cysts are referred to as merocytes. Attempts to produce infection in clean monkey by inoculation with the contents of the mature cysts failed entirely.

The tissue phase of development of *P. kochi* is accompanied by highly characteristic cellular reaction. The parasitized hepatic cell hypertrophies enormously with repeated nuclear division. There is no tissue response till the parasite reaches  $1\frac{1}{2}$  or more. Then large numbers of polynuclear leucocytes accumulate and make their way in between the cytoplasmic processes. This may progress till all trace of parasite is lost but in many cases the parasite continues its development. Then various cells of the lymphoid macrophage

system begin to accumulate between the parasite and liver parenchyma. There also appear large giant cells and phagocytic monocytes containing eosinophile granules. The parasite at this stage ruptures and its merozoites are scattered, while the remains of the parasite are invaded by the phagocytes. The site of the old schizont is represented on the liver by small fibrotic spots. Six mature schizonts gave average measurements of 1.8 by 1.3 mm.

Because of the peculiar character of the reproductive process with the production of the large spherical schizont with its central vacuole, the author believes that the parasite does not belong to the genus *Plasmodium*, nor does he agree with HAWKING and HUNT [this *Bulletin*, 1948, v 45, 494] that it belongs to the genus *Haemoproteus*. He accordingly employs the name suggested by LEVADITI and SCHOEN (*C R Soc Biol*, 1932, v 109, 343) naming the parasite *Hepatocystes kochi*.

The paper is illustrated by two coloured plates and two plates of photomicrographs. C M Wenyon

HAWKING, F, PERRY, W L M & THURSTON, June P. Tissue Forms of a Malaria Parasite *Plasmodium cynomolgi*. *Lancet* 1948, May 22, 783-9, 13 figs (7 on 1 pl) [18 refs]

In an earlier paper HAWKING described pre-erythrocytic schizogony of *Plasmodium cynomolgi* in the liver of monkeys after he had been shown these forms by SHORTT, who had found them in monkeys infected by injection of sporozoites [this *Bulletin*, 1948, v 45, 388]. The authors of the present paper give a fuller account of these experiments. They show that after the injection of sporozoites into monkeys the blood is infective to subinoculated monkeys for about 2 hours, after which it is non-infective for 7 days, 21 hours, when it again becomes infective. Study of the parasites which appear in the blood shows that the release of merozoites from the tissue forms is asynchronous and extends over three days. The number of parasites liberated varies from 1 million to 100 or 1,000 million, according to the infecting dose of sporozoites. The inoculation of emulsions of various organs of infected monkeys, including liver in which subsequent examination revealed pre-erythrocytic schizonts, failed to give rise to infections.

In sections of the liver of a 5-day monkey, the parasites measure on an average 12 by 14  $\mu$ . They lie in enlarged liver cells, the nuclei of which are unchanged or slightly increased in size. The chromatin masses in the parasite number about 70. In the liver of a 7-day 15-hour monkey, the average size of the parasite is 46  $\times$  31  $\mu$ . The largest form found measured 68 by 61  $\mu$ . In one cross-section there may be 100 to 250 masses of chromatin. Parasites very similar were found also in a 7-day 23-hour monkey. In most cases the parasites are roughly ovoid in shape, but sometimes they are quite irregular in outline and may show clefts in their cytoplasm or a tendency to segmentation into a number of separate masses which bear some resemblance to cytomeres. The host shows little tissue reaction to the presence of the parasite, but occasionally a parasite is invaded by polynuclear leucocytes. In one monkey inoculated intracerebrally with sporozoites, a form resembling a schizont was found in the brain. The paper is illustrated by twelve photomicrographs and a drawing showing variations in shape of a schizont in serial sections.

C M Wenyon

GRAMICCIA, G & BLACK, R H. The Cultivation of Exoerythrocytic Forms of *Plasmodium gallinaceum*. I. A Preliminary Note. *Ann Trop Med & Parasit* 1948, Apr, v 42, No 1, 88-9, 2 figs on 1 pl.

The method differs from that of HAWKING [this *Bulletin*, 1946, v 43, 410] in that infected organs for tissue culture were obtained from birds which had

received intravenous inoculation of blood containing trophozoites of *P. gallinaceum* instead of from birds which had been infected by sporozoites. Quinine (2.5 mgm) was given daily until parasites appeared in the blood, when the dose was doubled.

Typical exo-erythrocytic forms were found in the macrophage-like cells on the eighth day of the culture.

P. C. C. Gurnham

CLARK, Delphine H. & TRIFLER, M. Studies on Parasite-Host Interplay between *Plasmodium gallinaceum* and the Chicken as Influenced by Hydroxynaphthoquinones. *J. Infect. Dis.* 1948, Mar-Apr, 82, No. 2, 133-62, 5 figs. [40 refs.]

It is recognized that some drugs show different activity against the various stages in the developmental cycle of malarial parasites. A study of the action of 2-hydroxy-naphthoquinones on these different phases in *P. gallinaceum* infections of chickens is now reported with the object of elucidating some of the factors in the host and parasite which influence the activity of an antimalarial agent. The effect of the series of 2-hydroxy-naphthoquinones synthesized by FISKE, on carbohydrate metabolism and respiration of erythrocytic forms of *P. knowlesi* and *P. falciparum* was studied *in vitro* by WANDER (this Bulletin 1947 v. 44, 400).

The chemical constitution of the group differs from that of known antimalarials. In early observations on *P. gallinaceum* infections, it was found that they possessed activity against erythrocytic and exoerythrocytic forms and showed promise as prophylactic agents. The member of the group with which most of the present experiments were conducted was 2-hydroxy-3,5-decyl-1,4-naphthoquinone, which occurs in a number of stereoisomeric forms each of which may differ in antimalarial activity. In some cases a mixture preponderating in *cis*-forms was used.

Infection was induced in young chickens by graded intravenous inoculations of infected *Aedes aegypti* mosquito suspensions prepared by grinding up of parasitized blood, dosage being based on the size of the host. The course of the blood infection was followed in stained films and that of exoerythrocytic forms in smears of brain or by the method of COCHRAN *et al.* (this Bulletin 1945 v. 42, 629) as well as by subinoculation of fresh hosts. As a further test for utilization of infection in an experimental bird the method of superinfection was used. Drugs were administered in the diet in capsules or intramuscularly in an emulsion of peanut oil and sometimes intravenously and the level of the naphthoquinone were determined in plasma by spectrophotometric measurements on isoamyl alcoholic extracts of the highly coloured sodium salts.

When the drug was administered prophylactically prior to parasite inoculation of chickens parasites could not be detected in blood or brain smears by the methods outlined, in contrast to the results obtained with control or parasite-treated hosts. In subsequent experiment in which drug was given before sporozoite inoculation in the prepatent and also in the patent period it was shown to be very active on the earliest phases of the developing parasite and was less active against the phase present four days after infection. By careful timing of drug administration a long-term effect was obtained that the effect was against the sporozoite itself and complete prophylaxis was attainable. The naphthoquinone was also shown to be active against late exoerythrocytic forms of *P. gallinaceum*. Treatment of patent blood infections disturbed the mechanism of the developmental cycle and growth was retarded.

Comparison of the activities of the naphthoquinone, quinine and chloroquine (mepacrine) in blood-induced infections showed that all three reduced the number



of parasites in the peripheral blood, but differences in their activity were obvious when inocula of various sizes were used, the naphthoquinone being generally the more active and there was a maximal inoculum which could be controlled by each drug. The development of immunity was believed to play an important part in the "cures" obtained. The level of drug in the plasma influenced the rate of response to treatment. Chronically infected birds showed greater immunity than those treated early in the infection. The immune state of the latter appears to offer further opportunities for studying the factors affecting latency, relapse and cure in this infection. Therapeutic treatment involves an interplay between parasite, host and the agent used. The results described here are in general agreement with those of GINGRICH *et al* [this *Bulletin*, 1947, v 44, 803] who reported cures in canaries infected with *P. cathemerium* on treatment with the same naphthoquinone. [This careful and extensive analysis of the factors which come into play during treatment of the different phases of a malarial infection merit consultation of the original article.]

See also p 736, BLACK, Leishman's Stain adapted for Use with Histologic Sections

J D Fulton

RIGDON R H & McCAIN B E Effect of 3,3'-Methylenebis (4 Hydroxycoumarin) "Dicoumarol" on *P. lophurae* Infection in Ducks J National Malaria Soc 1948, Mar, v 7, No 1, 38-43, 2 figs

When dicoumarin (3,3'-methylene-bis-4-hydroxycoumarin) was given in repeated doses by mouth to young white Peking ducks infected with *P. lophurae* it was found that the degree of parasitaemia was reduced in comparison with controls. The development of a peak of parasitaemia was also delayed and deaths occurred earlier in these treated birds. In a typical experiment with a group of 40 ducks about 3 weeks old 10 were infected with *P. lophurae* and 15 others uninfected were given similar doses of the drug ranging from 25 to 100 mgm on 5 to 7 occasions. Parasite counts were made in the usual way in stained films. In the control animals anaemia, acidosis and haemorrhages in subcutaneous tissues were noted. Death appeared to be due to acidosis rather than anaemia and sometimes occurred rapidly in birds on low vitamin A intakes. The plasma was not coloured by haemoglobin but its CO<sub>2</sub> combining power was reduced. The drug is obviously of no value in treatment and the mechanism by which it produced the above effects is not known.

J D Fulton

WALKER, H A STAUBER, L A & RICHARDSON, A P Curative Action of Pamaquine Naphthoate, Quinacrine Hydrochloride, and Quinine Bisulphate in *Plasmodium cathemerium* Infections of the Duck J Infect Dis 1948, Mar-Apr, v 82, No 2, 187-96, 3 figs

Screening tests for antimalarials were widely developed during the late war with the use of a number of different host species and parasites. While many drugs showed suppressive activity, cures were less readily obtained. Two reports of tests for curative action have been described by KELSEY *et al* and by DEARBORN & MARSHALL [Proc Fed Amer Soc Exp Biol, 1946, 185, this *Bulletin* 1946 v 43 404] who used respectively *P. lophurae* infections of the chick and duck. The present authors now describe a curative test with *P. cathemerium* infections in the duck whereby certain drugs active in human malaria infections have been evaluated.

Peking ducks 10 to 12 days old of approximately 150 gm. were inoculated intravenously with  $5 \times 10^4$  parasites per kgm. of body weight. At the peak of infection on the 4th day 30 to 50 per cent. of the red cells were parasitized and by the 8th day parasites could not be found in thin films of peripheral blood of untreated fowls although it remained infective for fresh hosts over a period of some months. Different dosage schedules for each drug were used on 10 to 15 ducks one day before and for six days following inoculation. The drug diet method or stomach tube was used for administration. A regular 3 hour dark and 3-hour light cycle was automatically maintained. Blood smears from each host were examined one day after the end of treatment and weekly thereafter till the 30th day from inoculation or on death of a bird. At the end of the observation period fresh hosts were inoculated from the experimental birds and their blood was examined on alternate days for 15 days, a period regarded as suitable from other experimental observations. The donor birds were in turn inoculated with  $5 \times 10^4$  parasites per kgm. of body weight and blood smears were made 3 days later and the nature of the resultant infection, if any noted. Before a duck was regarded as cured, smears had to remain negative over the observation period and the bird subinoculated from it had to remain free from infection. Finally the challenging dose: the donor bird had to give rise to a normal acute infection. Subinoculation and reinfection were regarded as a more accurate index of cure than absence of parasites in the treated birds. A few discrepancies were however encountered in these two criteria in so far as both might be positive or both negative. In all, 147 ducks were treated with different drugs and 239 satisfied all three criteria: 1 cure. Pamaquin (plasmoquine) because of its properties was adopted as the standard in these experiments and effected a number of cures: so also did quinacrine (atebriol) but not quinine. Results with 8-aminoquinolines other than pamaquin suggested a correlation between the present results and those recently obtained in man.

J. D. Fulton

WALKER, H. A. & RICHARDSON, A. P. Potentiation of the Curative Action of 8-Aminoquinolines and Naphthoquinones in Avian Malaria. *J. National Malaria Soc.* 1948, Mar. 7 No. 1 411

Synergistic action between therapeutic agents of different chemical constitution against parasitic infections has frequently been noted. It is due possibly to the effect of these agents on different vital processes in the parasites. Such an action is now recorded in *P. cathemerium* infections of ducks between 8-amino-quinolines represented by plasmoquine (pamaquin) and pentaquine (SN 13,276) and three naphthoquinones (SN 5949, SN 12,320 and SN 13,836). Birds 10 to 12 days old weighing about 150 gm. were divided into groups of 10 to 20 and each was inoculated intravenously with  $5 \times 10^4$  parasitized cells per kilo of body weight from a donor bird. Drug-diet therapy at different dosage levels was started 16 to 18 hours before inoculation and continued for 6 days thereafter. Examination of the host blood for parasites was made at intervals for several weeks after infection. Following blood examination 23 days after inoculation, each host was re-inoculated with the same number of parasites as in the first instance and blood smears were examined three days later. Absence of parasites during regular examinations after treatment was used as one criterion, and the other which the authors consider more significant was the attainment of a sufficiently high level of parasitaemia after reinoculation. It was shown that pamaquin, pentaquine and SN 13,320 given alone were curative but the dosage required for 100 per cent. elimination of the infection was liable to produce fatal toxic effects. Pamaquin was more active than pentaquine, and showed about 20 times the activity of SN 13,320. Synergistic

effects were observed in various combinations of the two different types of drug in curative therapy, but were much less marked in suppressive therapy, suggesting that the mechanism in the two cases was different. From other experiments it appeared that SN 12,320 alone was more effective in the cure of well-established infections. The value of similar combinations to the above in the treatment of human malaria, as well as the mechanism by which the effect is produced, has yet to be determined.

J D Fulton

## TRYPANOSOMIASIS

### ERRATUM

In the *Summary of Recent Abstracts, Trypanosomiasis*, this *Bulletin*, 1948, v 45, at the foot of page 383, the following sentence "The author [VAN HOOFF] thinks that melarsen oxide is useful for the treatment of patients with resistant strains (a conclusion not shared by LOURIE)" does not correctly represent the views of Lourie, who shows, on p 413 of the same issue, that he has confirmed van Hoof's findings. The phrase in brackets, therefore, should be deleted.

Charles Wilcocks

NASH, T A M A Note on the Effect of High Temperature on the Pupal Stage of *Glossina* in relation to the Transmission-Rate of Trypanosomes. *Ann Trop Med & Parasit* 1948, Apr, v 42, No 1, 30-32

In BURTT's experiments [this *Bulletin*, 1946, v 43, 827, 1947, v 44, 803] tsetse flies (*Glossina morsitans*) which hatched from pupae incubated at about 86°F showed a greater transmission rate for *Trypanosoma rhodesiense* than those hatched from pupae kept at the lower average temperature of the laboratory. In Northern Nigeria, NASH [this *Bulletin*, 1942, v 39, 532] found many pupae of *G. submorsitans* in soil at temperatures ranging from 69° to 82°F but very few at higher temperatures, and as the shade temperature reached 106°F (probably as high as anywhere in Africa) it is probable that BURTT's pupae were incubated at a higher temperature than they would experience in nature. his experiments should be repeated to compare the effect of temperatures of 68° and 82°F.

The author's work in Nigeria [see also this *Bulletin*, 1937, v 34, 533, 1940, v 37, 15] led him to conclude tentatively that most sleeping sickness conveyed by the riverine tsetse flies *G. palpalis* and *G. tachinoides* is contracted in the late dry season when the soil temperature is high and when the flies have become restricted to permanent water pools such as the village water holes here in contact between the flies and the people is close and the flies are compelled to feed largely on human beings. Confirmatory evidence for this view was not obtained from the dispensaries as the disease is mild in character and the people present themselves late for treatment. If it should be confirmed it may be possible to reduce the length (and cost) of protective clearings of river crossings to that required for the dry season only.

J F Corson

KLEINE, F K Unterschiede in der Bekämpfung der afrikanischen und der russischen Trypanosomiasis [Differences in the Control of African and Russian Trypanosomiasis] *Ztschr f d Deut Gesundheitswesen* 1946 v 1, No 6, 143-4

Domestic animals in southeastern Russia, where camels are much used in agriculture, are infected with surra (*Trypanosoma evansi*), as the trypanosome-

is directly and mechanically carried from one animal to another by tabanid and other biting flies which do not themselves become infected, the control of surra would seem to be less difficult than that of those African trypanosomes transmitted by tsetse flies which become infected and form an additional reservoir of the trypanosomes. The author refers briefly to the various well-known methods of controlling trypanosomiasis in man and animals.

As *T. cruzi* and *T. brucei* resemble each other so closely in appearance it is thought that they are nearly related, but the former apparently cannot develop in tsetse flies. HUNERT and KRAUSE [this *Bulletin* 1934 v 31 597-1935 v 32, 362] failed to infect *Glossina morsitans* with a strain of *T. cruzi* isolated less than a year previously. [As was noted by the reviewer of their papers the direct transmission of *T. cruzi* by *G. morsitans* as late as the 3rd and 5th days after they had fed on an infected animal is remarkable. Further experiments on direct transmission of pathogenic trypanosomes are desirable.]

J. F. CORRIE

KENEFORD J. R. LOURIE, E. M. MORLEY J. S. SIMPSON J. C. E. WILLIAMSON J. & WRIGHT P. H. Cinnoline Derivatives as Chemotherapeutic Agents for *Trypanosoma congolense* Infections. (Correspondence) *Nature* 1948 Apr 17 603-4

The authors have synthesized quaternary salts of various mono- and diamino-cinnolines, -quinazolines and -quinolines in which substituent amino groups can be more readily introduced than is the case with the more complex phenanthridinium compounds of the type described by BROWNING *et al.* [this *Bulletin*, 1938 v 35 344]. The latter compounds, especially dimethyldiam bromide (1533) and phenidium chloride (697) are the most active substances so far described for the treatment of *T. congolense* infections in cattle in Africa. Two substances, 4,6-diamino-1-methylcinnolinium iodide and a derivative with an imine in position 3 were found to be inactive against *T. congolense* in cultures in mice when pure whereas the impure products of reduction had comparable activity to that of 697 but were much less active than 1533. The impurities in the two compounds were believed to arise from side reactions during reduction of the 6-nitro precursors and are possibly comparable with symmetrical structures. Attention is drawn to the trypanocidal activity of certain other non-aromatic compounds with symmetrical molecules. Analogous activity of symmetrical sex hormones suggests that symmetrical compounds with the type of structure suggested for the above active products may provide useful trypanocides.

J. D. FALLO

WILSON S. G. Further Observations on the Curative Value of Dimethyldiam Bromide (Phenanthridinium 1533) in *Trypanosoma congolense* Infections in Uganda. *J. Comp. Path. & Ther.* 1948 Apr. Vol. 60 No. 1

HARVEY S. C. Sulfhydryl and Disulfide Content of Normal and Antimony-Resistant Trypanosomes. *Proc. Soc. Exper. Biol. & Med.* 1948 Mar. v 67 No. 3 269-72. 1 ref.]

VOEGTLI and co-workers [this *Bulletin* 1944 v 41 414-1945 v 42 106] showed that the -SH group was present in certain trypanosomes and suggested that polyvalent arsenical was capable of combining with it. It was suggested that a similar group may also combine in the same way. The active principle of the tripeptide glutathione which in the reduced form contains a free -SH group, was believed to play a part in the pharmacology of antimony-resistant trypanosomes. A quantitative estimation of sulfhydryl

groups (capable of yielding the former on reduction) in normal and arsenic-resistant strains of *T. equiperdum* and *T. hippicum* was therefore made, in order to test the truth of the above view. For this purpose, the trypanosomes were obtained free from red cells by centrifuging the blood of infected rats. The washed preparation was mixed with 15 per cent trichloroacetic acid and the solid obtained on centrifuging was resuspended and treated in the same way. The product was then suspended in dry acetone and shaken with the addition of a drop of concentrated HCl. After centrifuging the same process was repeated. On removal of the liquid *in vacuo*, the residue was ground to a fine powder and dried at 105°C for 30 minutes. The method of MURSKY and ASSON (*J Gen Physiol*, 1935, v 18, 307) was used for the estimation of -SH groups before and after reduction and the content of -S-S- groups present was obtained by difference. The values for the -SH groups present in normal and arsenic-resistant forms of both species of trypanosome showed differences which were not regarded as significant. The normal strain of *T. equiperdum* however contained an excess of disulphide groups compared with the resistant form, while in the case of *T. hippicum* the reverse was the case. There was no indication of a definite relationship between actual and potential -SH content of the trypanosomes and arsenic-resistance, and on this basis also no explanation was forthcoming why certain arsenicals with an acidic side chain are effective against arsenic resistant forms.

J D Fullon

CHEN, G & GEILING, E M K. The Effect of Cysteine on the Antitrypanosome Activity of Antimonials. *J Infect Dis* 1948, Mar-Apr, v 82, No 2, 131-2.

The authors [this *Bulletin*, 1945, v 42, 869] showed that the trypanocidal activity and toxicity of trivalent, but not of pentavalent antimonials, for mice, was reduced by cysteine. The inhibitive effect of both types of compound on glucose metabolism of the trypanosomes was also antagonized by this substance *in vitro*. The effect on the trypanocidal activity of tartar emetic, sodium-antimony-thioglycollate, stibamine and neostibosan as judged by sugar metabolism *in vitro* has now been investigated by the methods previously described [this *Bulletin*, 1946 v 43, 315]. Cysteine hydrochloride brought to pH 7.5 by trisodium phosphate was added to the trypanosome suspension at different intervals of time after the administration of the drug during the observation period of 1 hour. It was found that cysteine was able to antagonize the inhibitive effect of both the trivalent and pentavalent compounds on the glucose metabolism of *Trypanosoma equiperdum*. Experimental data in the case of stibamine indicated that there was a lag in the effect produced by this drug on trypanosome metabolism, in agreement with the delayed toxic effects produced by the same substance in mice compared with trivalent compounds. The possibility that the pentavalent antimonials exert their trypanocidal activity after reduction has frequently been suggested, but proof is still lacking.

J D Fullon

CHEN, G. The Effect of Methyl-Bis ( $\beta$ -Chloroethyl) Amine on *Trypanosoma equiperdum*. *J Infect Dis* 1948, Mar-Apr, v 82, No 2, 133-7, 1 fig.

The effect of methyl-bis ( $\beta$ -chloroethyl)-amine (nitrogen mustard) on the glucose metabolism, morphology, motility, survival and reproductive powers *in vitro* of *T. equiperdum* has been investigated.

The effect of cysteine hydrochloride brought to pH 7.5 by trisodium phosphate was tested as an antagonist of the action of this drug. The methods for studying glucose metabolism have been described [this *Bulletin*, 1946, v 43, 315]. After

the drug in suitable medium had been mixed with heparinized blood from an infected rat, the effect on reproduction was investigated by studying the number of dividing forms present in stained smears. Those with two parabasal bodies were put in this category. The infectivity for mice of trypanosomes kept in a concentration of the drug, which over a period of 1 hour did not produce any morphological changes, was also determined after centrifugation and replacement of the medium. The effect of the nitrogen mustard on the course of the infection in rats was also studied, but the substance proved very toxic for these animals. An inhibitive effect on glucose metabolism was shown by a  $10^{-3}$  molar concentration of the drug which is therefore less effective than tartar emetic or stibamine. With 5 times the above concentration, motility of the trypanosomes in suspension was impaired after 1 hour without significant reduction in numbers and their morphology was at that time unaltered, but some change was evident after two hours. Dividing forms were reduced in number after exposure to a  $5 \times 10^{-4}$  molar concentration of the drug for 2 hours. The specific effect on the reproduction was shown by inoculating mice which had been subjected to different molar concentrations of the drug for 1 hour. From the increased survival time of the infected animals the minimal effective molar concentration of drug appeared to lie between  $10^{-5}$  and  $10^{-6}$  while a maximal effect was produced at  $10^{-3}$ . The mechanism of the effect on multiplication was studied by investigating the relationship between the dose of treated trypanosomes and the survival time. It appears that certain phases of mitosis are inhibited. Cystene was able to antagonize the effect of the nitrogen mustard.

J. D. Fuller

MALINOFF, W. M. The Action of the Endotoxin of *Trypanosoma cruzi* (SR) on Malignant Mouse Tumors. *Source*, 1947 Dec. 12, 501-4 2 figs.

### LEISHMANIASIS

GHOSH, H. & GHOSH, N. V. Complement-Fixation Reaction in Sera of Rabbits actively immunized with Living Culture of *Leishmania donovani*. *Ann. Biochem. & Exper. Med.* Calcutta, 1947 v 7 No. 1/4 12.

— & — Agglutination Reaction in Sera of Rabbits Immunized with different Strains of *Leishmania donovani*. *Ibid.* 3-8. (11 refs.)

Three rabbits were immunized by intra-venous injection of live cultures of *Leishmania donovani* six times at intervals of four days. The dose of organisms was 100 million increased to 1 000 million.

In the first paper the titre of the complement fixing antibodies is given as 1 in 8,000 1 in 6,000 and 1 in 14,000. The complement fixation reaction was carried out with an emulsion 1 flagellates in 0.25 per cent phenol in distilled water the emulsion containing 60 million organisms per cc.

In the second paper the agglutination reaction of the sera is described. Various antigens were prepared from culture flagellates. The titres of the immunized sera were 1 in 24,000 1 in 16,000 and 1 in 32,000. There appears to be no H or O antigen in *Leishmania donovani*. C. M. Henry.

LUMITZ, J. M. Pathology of Kala-Azar. Report of a Case. *Am. J. Trop. Med.* 1946, Mar., v 23 No 2, 275-83 8 figs. (11 refs.)

The author gives a short review of the pathology of kala azar and reports the autopsy findings in one case.

The subject was an East Indian seaman from Calcutta. Diagnosis was made by sternal puncture. A spleen puncture was also performed and the man died six hours later. The clinical aspects of this case have been reported previously [this *Bulletin*, 1947, v 44, 986].

The abdominal cavity contained about 4,000 ml of bloody fluid. There was a small round puncture hole on the convex surface of the spleen about 2.0 mm in diameter. No blood clot or fibrinous deposit was seen on the capsule. The spleen weighed 1,030 grammes. The capsule was tense and the friable red pulp bulged above the cut surface. The liver was flabby and soft and the cut surface had a nutmeg appearance. There was a large area of broncho-pneumonia in the upper lobe of the right lung and scattered foci in the lower lobe. Small superficial ulcers surrounded by minute haemorrhages were noted in the rectum.

Microscopic examination of the spleen showed atrophic and scanty Malpighian follicles and highly cellular red pulp with enlarged and rounded reticular cells, some of which were parasitized. There were fatty changes in the liver parenchyma cells and hyperplasia of the Kupffer and interstitial cells, parasites were seen in the latter. In the bone marrow there was increased cellularity, the bulk of which was "clasmocytic tissue", many leishmaniae were seen. Leishmaniae were not found in the lymph glands or in other organs and tissues.

In the brain, there was a 'ring haemorrhage' in the basal ganglia and a small focus of gliosis in the pons. It was not decided whether these changes were due to kala azar or to some other conditions.

There are 7 good photomicrographs, and one photograph showing the cut surfaces of the liver and spleen.

L. C. Napier

CARTWRIGHT, G. E., CHUNG, H. L. & CHANG, A. Studies on the Pancytopenia of Kala-Azar. *Blood* 1948, Mar, v 3, No 3, 249-75, 13 figs [39 refs].

The authors commence with a summary of the previous work on the blood picture in kala azar. The summary is a comprehensive one as far as work in China is concerned.

The present study is based on findings in 143 cases of kala azar diagnosed by the demonstration of *Leishmania donovani*, of these, 27 were studied in great detail and the analysis of the findings in these cases forms the main body of this paper.

Anaemia was constant. The average haemoglobin for 124 uncomplicated cases was 8.3 grammes per cent. In one-third of the patients it was below 7 grammes per cent. The anaemia was significant (10.6 grammes), it occurred immediately after the onset of symptoms and was subsequently progressive. There was a positive correlation between splenic enlargement and anaemia.

The anaemia was normocytic orthochromic. Leucopenia was an almost constant feature of uncomplicated kala azar. The average white cell count of 124 patients was 2,835 per cmm. Only 16 patients had a white count above 5,000 per cmm. The leucopenia was apparent at the time of onset of the symptoms and it increased slightly in intensity with the progress of the disease. There was a correlation between a low white cell count and splenic enlargement.

The platelets were reduced in the majority of cases, the average in uncomplicated cases was 103,000 per cmm (330,000 being normal by this method). The thrombocytopenia developed later, it was not usually present until two months after the onset of symptoms, but was progressive subsequently. In the presence of severe complications, e.g., noma, the thrombocytopenia was more marked.

The bone marrow was always hyperplastic, reticulo-endothelial cells constituted 5 to 50 per cent of the total cells, but all the blood-forming cells were present, and the authors consider that the reticulo-endothelial proliferation is

mainly at the expense of the fat. The proportion of reticulo-endothelial cells tends to increase with the duration of the disease. One to 60 per cent. of the reticulo-endothelial cells were parasitised.

A table shows the bone-marrow differential counts in 27 cases. Poly-morphonuclear leucocytes were reduced from the normal of 20 per cent. to a mean of 3.4 per cent. in the 18 uncomplicated cases. This change develops within the first month of the disease. The eosinophils were also markedly reduced—they were often absent in a count of 500 to 1 000 cells. The erythroid cells were increased from a normal of 22 per cent. to 36 per cent. of all cells except reticulo-endothelial cells. The leucocyte-erythroid ratio is shifted from 3.5:1 to an average of 1.8:1.

The number of megakaryocytes was sometimes greater than normal, sometimes less—the average was slightly less than normal, i.e. 122 per million nucleated cells, but platelet production was markedly reduced. Few clumps of platelets were to be seen in the marrow. In the treated cases, there was active platelet production and there were usually more masses of platelets than are seen in normal marrow although in the peripheral blood the platelets were still short of normal.

The lymphocytes and monocytes were present in approximately normal numbers, but the plasma cells were somewhat increased.

During effective anti-leishmanial therapy parasitised reticulo-endothelial cells disappeared and the percentage of reticulo-endothelial cells gradually diminished as the polymorphonuclear neutrophils increased. There was a significant increase in the eosinophilic cells. Lymphocytes became more numerous and the plasma cells diminished in number. Nucleated red cells became less numerous and the leucocyte-erythroid ratio returned to normal. At the same time the proportion of orthochromatic normoblasts to polychromatic normoblasts increased. The three cellular elements were restored to normal in the peripheral blood in the same order as their reduction from normal.

Evidence is presented which contradicts the view that the pancytopenia is due to a crowding out of the bone-marrow by reticulo-endothelial cells.

Certain similarities between the haematological changes in this disease and those accompanying the hypersplenic syndromes are noted. *L. E. N. J. pier*

SANCHEZ HAYARIZ, V. SELVA, J. & MARCO VENTURA, R. Formulas hematológicas anormales en el kala-azar. [Unusual Blood Findings in Kala Azar.] *Med. Colonial, Madrid*, 1948 May 1 v 41 No. 5 383-8.

An account of two cases and a discussion on leucocytosis in kala azar.

HO E. Y. SOONG, T. H. & LI Y. Comparative Merits of Sternum, Spleen and Liver Punctures in the Study of Human Visceral Leishmaniasis. *Tr. R. Soc. Trop. Med. & Hyg.* 1948 Mar v 41 No. 5 629-33.

In a series of 450 cases of kala azar an attempt was made to appraise the value of the diagnostic methods, spleen, sternum and liver puncture, before treatment. Punctures were performed in other cases during and after treatment with urea stibamide.

The techniques are described shortly. smears, stained by Wright's stain, were examined.

In a series of 450 cases finally diagnosed as kala azar in which spleen and liver punctures were performed before treatment both punctures were positive in 375 (83.4 per cent.) spleen puncture only was positive in 64 (14 per cent.) and sternum puncture only was positive in 11 (4 per cent.). Among the



375 cases in which both punctures showed leishmania, larger numbers were shown in the spleen puncture material in 184 (49.1 per cent) and in the sternum puncture material in 34 (9.1 per cent).

In 121 cases of the same group liver puncture was also done. Of these, in 118 (97.6 per cent) spleen puncture was positive, in 108 (89.2 per cent) sternal puncture was positive, and in 93 (76.9 per cent) liver puncture was positive. In no instance was liver puncture alone positive.

In a series of 203 cases in which the punctures were performed during treatment, leishmania disappeared from both spleen and bone marrow at the same time in 138 (68.0 per cent) instances, in 41 (20.2 per cent) instances the spleen puncture was negative while the sternum puncture was positive and in 24 (11.8 per cent) instances the reverse was the case.

In another 86 cases under treatment, parasites disappeared from the spleen, liver and sternum at the same time in 45 instances, while in the remaining cases they disappeared from the liver first.

After treatment, the "sternum and spleen punctures were found to check up each other very closely."

The authors recommend that both spleen and sternum puncture should be performed to ensure accurate diagnosis. They consider that "once the technique is mastered, spleen puncture is the simplest of the three, but it is not so certain as sternum puncture, especially since the latter can be repeatedly tried without risk at one session." [This statement is not understood.]

There were no ill-effects from the punctures performed in any of their cases.

TRINÇÃO, C. A New Reaction for the Diagnosis of Kala-Azar. *a Preliminary Report Amer J Trop Med* 1948, Mar, v 28, No 2, 287-8.

While estimating iron in serum, the author noted that when 1 part of hydrochloric acid (0.3N) was added to 2 parts of serum of a kala azar patient, after a short interval the mixture became coagulated in a manner that reminded him "of the phenomenon demonstrated by the well-known formic aldehyde reaction of Napier."

On addition of the hydrochloric acid there is "an immediate slight cloudiness and when the reaction is complete, the jellified serum may take on a darker tinge its initial cloudiness is increased, and, though continuing translucent, it assumes a slightly milky appearance."

The author tried this reaction in four other cases of kala azar, one in an advanced stage of treatment, the rest clinically cured. The first case gave jellification of the serum at the end of 24 hours and all produced a soft jelly. The author has made hundreds of serum-iron determinations and in no other cases has the reaction occurred, except that in a case of multiple myeloma (aldehyde test=++) the serum jellified after 24 hours.

SNOW, J S SATULSKY E M & KEAN B H. *Amerleian Cutaneous Leishmaniasis Report of Twelve Cases from the Canal Zone Arch Dermat & Syph* 1948, Jan, v 57 No 1, 90-101 2 figs [Refs in footnotes]

Cutaneous leishmaniasis is uncommon in the Panama Canal zone, only 18 cases have been observed at the Gorgas Hospital since 1904. Of these, 6 were prior to 1937, the remaining 12 cases are included in this report. Very few cases have been reported in the Republic of Panama outside the Canal zone, two references to reports on 8 such cases are given. In 9 of the 12 cases the lesions appeared first in the dry season, January to March. All the patients were males. Six were soldiers from the United States.

and three from Porto Rico. Three were labourers, 2 being Panamanians and one a Colombian.

"All patients had been in the Isthmus of Panama for several months before the appearance of the lesions, so that there is little doubt that they were autochthonous." The estimated incubation period was less than 2 weeks in 4 cases and less than a month in two others.

In nine cases there were single and in three multiple lesions.

The lesions were all on exposed parts of the body. All started as irritating "insect bites" which the patient scratched. All cases presented open ulcers, 0.5 to 9.0 cm. in diameter. The ulcers had raised sometimes undermined borders with bases of granulation tissue. There was usually a copious thick serous discharge but occasionally a purulent discharge. "A striking feature was the occurrence of multiple small subcutaneous nodules along the regional lymphatics. In 3 of the 8 patients with lesions of the upper extremity. Most of these showed no inflammatory reaction. Regional lymphangitis and adenitis were also usual.

The histopathology is described in detail. It was noted that the cellular reaction in the subcutaneous nodules resembled closely that seen in the biopsy of the ulcers. Leishmania were found in the latter in each case usually in macrophages but occasionally in epithelial cells, but were not found in the nodules. However some treatment had been given in all the cases examined.

Treatment was by potassium antimony tartrate, Stibophen (Fouadin) or stibamine glucoiside (Neostam) intravenously. Immediate (coughing, vomiting and chill) and late (joint pains) reactions occurred with all the drugs, but were most marked with potassium antimony tartrate. Improvement occurred within a week and the average healing time was 5-7 weeks. If the severity of the case was taken into consideration, there was little difference between the results obtained with the three drugs.

L. E. A. FRY

PERRAIA, S. B. & ROTBERG, A. Nota sobre o tratamento intensivo da leishmaniose tegumentar americana pelo tartarato de sódio antimonila. [Intensive Tartar Emetie Treatment of American Cutaneous Leishmaniasis.] *Hospital, Rio de Janeiro*. 1947 Dec. v. 22, No. 6 845-52 10 figs.

The authors, following the experience of ALVES and BLAIR [this *Bull.* 1946, v. 43, 344] in the treatment of schistosomiasis by intensive administration of tartar emetic have tested the method in six cases of S. American cutaneous or mucocutaneous leishmaniasis. The solution used was put up in ampoules each containing 0.13 gm. of the salt in 10 cc. 1 normal saline with 5 per cent. glucose. Three ampoules were administered each day for two days, a total of 0.78 gm. being given in the six injections. In most cases the full course was repeated a second or a third time after three or four weeks. In some cases a modified course was given. The improvement noted in some of the cases would seem to justify further tests of this intensive treatment.

C. M. Wray

## FEVERS OF THE TYPHUS GROUP

MACCARTHY Ethna. Public Health Problems created by Loose Infestation. *Irish J. Med. Sci.* 1948 Feb 6th ser. V. 20: 65-78, 2 L., & 4 maps. [14 refs.]

Among more than 5,500 persons coming from all the counties of Eire for the examination prescribed in the Health Embarcation Scheme for emigrants, high rates of loose infestation were found.

Among men, the percentage of infestation with body lice or their nits ranged from 30 to 65 per cent in the different counties, for women the rates were considerably lower, but they refer only to the discovery of live lice and the real rate of infestation was believed to be as high as among the men. Head lice were found in 40 to 100 per cent of the women from different counties.

Out of 401 persons tested by the Weil-Felix reaction, 154 reacted at 1-25 or over against *Proteus OXK*, against *P OX19* and *P OX2* the corresponding reactions were 33 and 37 respectively. The percentages of reactions among persons from "endemic" and "non-endemic" areas were much the same, except for the *P OXK* reaction which was nearly three times more frequent in persons coming from the non-endemic areas.

A titre of 1-125 was reached in only 12 cases, in eight of which the reaction was with *P OXK*, two reactions of this titre occurred with each of the other two strains, including one at 1-250 against *P OX2*.

Two interesting family outbreaks of typhus are mentioned. One of these occurred in Drogheda in 1939 [thus *Bulletin*, 1942, v 39, 138], and it was found that every person attacked had engaged in unpacking trunks which contained clothing belonging to "old ladies who had been the sole survivors in their street of an epidemic in 1898". The other outbreak, in Galway in 1926, affected persons who in a search for firewood had broken into an old shack which had remained closed for 15 years since the death, in one day, from typhus fever, of a family of five. The shack contained only one bed. In neither outbreak was there any further spread of the disease and it appeared likely that the infection was caused by dust in which virulent rickettsiae had survived for periods of 41 and 15 years.

John W D Megaw

GIROUD, P & JADIN, J. Diagnostic différentiel des typhus par l'agglutination des rickettsies [The Differential Diagnosis of the Typhus Fevers by Rickettsia-Agglutination. *Bull Soc Path Exot* 1948, v 41, Nos 1/2, 20-25]

The authors state in general terms their reasons for regarding the rickettsia-agglutination test as preferable in ordinary circumstances to the complicated complement-fixation test, as well as to the Weil-Felix and precipitin tests. They claim that the rickettsia-agglutination test of P and M-L GIROUD easily differentiates between epidemic and murine typhus during the 3rd and 4th days of attacks and also after the height of the attacks. The difference between the epidemic and murine titres is less pronounced in the intermediate stage and also when the sera have been inactivated by heating or have been stored for long periods.

John W D Megaw

HIRSZFELD, L. Notes on New Methods in the Investigation of Typhus Fever. *Texas Reports on Biol & Med* 1948, v 6, No 1, 21-2

This work was begun during the German occupation of Warsaw and was temporarily discontinued in 1942, owing to the war.

The author isolated 30 strains of *Proteus X* from blood, urine and postmortem material of typhus patients with the use of Mueller-Kaufmann medium containing ox-bile. The best results were obtained from the inoculation of each tube of medium with 1 to 2 cc of blood from the patient during the second week of the disease. A series of a dozen inoculations from each case is recommended. After 24 to 48 hours' incubation, transfer is made to agar. The strains isolated were agglutinated by the patients' sera in dilutions four times higher than was the case with a standard *Proteus X19* strain.

It was found that the sensitization of red cells influenced their absorption capacity on filter paper. This was applied, apparently with success, in the

cultivation of *Proteus X*. Serum from a typhus patient was added to his urine, which was filtered. Strips of the filter paper were then submerged in the Mueller-Hauffmann medium and in a large proportion of our cases *Proteus X* was cultivated."

During this investigation it was found that if patient's serum in decreasing amounts of 0.5-0.4-0.3-0.2-0.1 and 0.05 cc. was added to five tubes each containing 2.5 cc. of patient's urine, a precipitate was formed "in certain dilutions after 15 minutes but although this "uroprecipitation" test first seemed to be specific for typhus, it later gave positive results in typhoid and scarlet fevers and also certain anomalous results were found. The author suggests that if uroprecipitation indicates a specific substance there might be also another factor of overlapping antigenicity or an appearance in the urine of substance as a result of colloidoclasia." [This paper is extremely brief and further confirmatory details of the results described would be required before a critical opinion could be offered on them.]

H. J. O'D. Burke-Gaffney

BERCEANU S. & CUCURURANU Iulia. Studiu asupra turburărilor nervoase din tifosul exantematic. Forme clinice speciale [Nervous Manifestations in Exanthematic Typhus. Special Clinical Types.] *Rev. Științelor Med.* Bucharest, 1947 Nov-Dec, v. 38 Nos. 11/12, 484-502. French summary.

During the course of an epidemic of typhus in Bucharest in 1943 230 cases were examined by the authors. In 141 of these, nervous symptoms dominated the clinical picture. Confusion was observed in 33 cases, dysarthria in 15, deafness in 17, blindness in 1, strabismus in 1 and mydriasis in 2 cases. 3 cases were bulbar and 16 meningeal in type. In all 230 cases there was some degree of cellular reaction in the cerebrospinal fluid. This was often slight in the presence of severe meningeal symptoms, and these cases formed a well-defined type of serous meningitis. A type was also seen where symptoms were predominantly those of compression due to cerebral oedema or increased pressure of the cerebrospinal fluid. These cases included 3 of hemiplegia and one with cerebellar symptoms.

D. J. Bauer

HORTOPANU D. Pronosticul tifosului exantematic. [The Prognosis in Epidemic Typhus.] *Rev. Științelor Med.* Bucharest, 1947 Nov-Dec, v. 38 Nos. 11/12, 510-71. [15 refs.] French summary.

Case mortality from epidemic typhus in Rumania has fallen considerably for several decades and in 1946 it was below 10 per cent compared with 20 to 50 per cent in the last century.

During the recent war 463 cases were studied by the author and he believes that this improvement is due not to any epidemiological change as such, but to the better standards of life of the European populations, to progress in hospital organization and care of the sick, and markedly to the part played by sulphonamides and penicillin in reducing mortality attributable to complications.

Where nutritional and physiological states were low as was seen among refugees and prisoners of war the disease was of course more serious and the mortality higher. In famine typhus it has exceeded 20 per cent.

In a table, the author shows that a very important factor in causing death during typhus is the age of the patient. In his own records, 31 per cent of deaths occurred in those over 40 years and 50 per cent in those over 50. The exceptional gravity of typhus in those past middle age is stated to be due to existing arteriosclerotic lesions, which contribute to the serious complications.

of the disease itself, this arteriosclerosis is localized in just those organs in which the acute local lesions of typhus are to be found, *e.g.* the myocardium, brain and kidneys. The author, describing typhus as a "*maladie essentiellement artériolaire*", suggests that "the prognosis of epidemic typhus is inscribed on the patients' arteries". He regards a rising blood urea as an important sign in diagnosis and prognosis.

The prominent sequelae of epidemic typhus according to the author, are cerebral lesions, amputations for gangrene of the limbs, myocarditis and permanent mental disabilities, but in his experience such sequelae are not common and rarely exceed 1 per cent.

H J O'D Burke-Gaffney

ANIGSTEIN L, WHITNEY, Dorothy M & BENINSON, J. Inhibition of Typhus and Spotted Fever in Guinea Pigs by Intradermal Inoculation of Antiorgan Sera and of certain Normal Sera. *Texas Reports on Biol & Med* 1948, v 6, No 1 87-96 [15 refs]

The serum of rabbits which had been inoculated with the spleen and bone marrow of guineapigs contains antibodies against these organs, and is called antiorgan serum. An area of the skin of each of several guineapigs was infiltrated with this serum and after two hours the centre of the area was inoculated with brain substance of guineapigs infected with typhus and "spotted fever" [Rocky Mountain spotted fever]. Evidence of active infection was usually absent except for a few animals which suffered from greatly attenuated attacks. The serum of normal rabbits occasionally caused an attenuation of infection in guineapigs inoculated in similar conditions.

The interpretation of the barrier effect produced by the antiorgan serum is discussed and it is suggested that the production of a macrophage reaction by the serum may play an important part. The authors state that they can offer no suggestion as to the possibility of applying the results of their experiments to the prevention or treatment of typhus infections.

The original paper should be consulted by those interested in the problem of the protective action of antiorgan sera.

John W D Megaw

ANIGSTEIN L, WHITNEY, Dorothy & BENINSON J. Inhibition of Typhus and Spotted Fever by Intradermal Inoculation of Antiorgan or certain Normal Sera. *Proc Soc Exper Biol & Med* 1948, Jan v 67 No 1 73-4.

This is an abbreviated form of the above paper.

PLOTZ H, BENNETT B L, WERTMAN, K, SNYDER, M J & GAULD R L. The Serological Pattern in Typhus Fever. I. Epidemic. *Amer J Hyg* 1948, Mar v 47 No 2, 150-65, 2 figs [14 refs]

This important paper contains the substance of four confidential reports submitted in 1944 to the Surgeon-General of the U.S.A. Army.

Most of the work described was done by Col Harry Plotz, whose death in 1947 is deeply regretted.

A detailed study was made of serological reactions on sera collected every two days from 32 confirmed cases of epidemic typhus fever treated at Cairo in the winter of 1943. In attempts to recover rickettsiae from 23 of the patients, 21 strains of epidemic rickettsiae were isolated.

Strictly specific epidemic and murine antigens were prepared from yolk-sac rickettsial cultures by a modification of Craigie's method, in which the soluble non-specific antigens were removed by ether treatment combined with repeated

washing in saline of the rickettsiae deposited by centrifugation. The suspensions were preserved by the addition of formal to 0.2 per cent. Details of the technique employed are given in full for the first time.

The washed antigens gave no reactions with sera of patients or guinea-pigs convalescent from Q fever Rocky Mountain spotted fever boutonneuse fever, scrub typhus, and various other infections.

The antigens, after titration, were employed in a systematic series of complement fixation and rickettsia-agglutination tests of which complete details are given in the paper.

The following extract from a table shows the average titres observed at various stages of the illness.

Day of Illness	Complement Fixation (Epidemic antigen)	Rickettsia-Agglutination	
		(Epidemic antigen)	(Murine antigen)
2-5	0	10	0
6-7	5	40	10
8-9	20	320	60
10-19	640	10,240	1,260
20-30	320	2,560	640
31-60	80	640	80

Titres for the complement fixation tests with murine antigen are not shown in the table, but from the complete data it appears that they were much lower than those with epidemic antigen except in one case in which they remained the same till the 14th day on which both were 1-40.

Complement-fixing antibodies of epidemic typhus usually appeared about the 6th or 7th day. In every case they were present before the 16th day.

Rickettsial agglutinins appeared earlier with epidemic antigens, no negative reactions were ever observed after the 7th day.

By both tests differentiation between epidemic and murine typhus was always possible. The chief value of the agglutination test was the earlier appearance of positive reactions, but there was a greater degree of cross-reaction than with the complement fixation test, with which in 18 cases the reaction against murine antigen remained negative throughout the illness, and in only four cases did the titres exceed 1-40.

With the Weil-Felix test (OAV) a titre of 1-80 was reached in 26 cases by the 8th day and in the rest by the 11th day but, of course the test did not help in differentiating epidemic from murine infection.

John W. D. Morgan

SCOVILLE, A. B., JR., BENNETT, B. L., WERTMAN, H. & GAULD, R. L. The Serological Pattern in Typhus Fever. II. Murine. *Amer J Hyg* 1943, Mar., v. 47 No. 2, 168-78 2 figs.

This paper is complementary to the preceding one. It contains the results of serological tests carried out in the same way on sera obtained from 13 patients during an outbreak of murine typhus in September 1944 in Tennessee. Murine rickettsiae were isolated from eight of the patients.

The results obtained, *mutatis mutandis*, were generally similar to those reported in the preceding paper except that the differential diagnosis between epidemic and murine typhus could not be made so early a stage.

The murine rickettsia-agglutination reaction was still negative in four of the ten patients tested on the 5th and 9th days, but no negative reactions occurred after the 9th day.

The murine complement-fixation reaction with washed antigen was still negative in 12 cases in tests carried out on the following days of the illness — 10th, 11th (3 cases), 13th (5 cases), 15th 16th and 19th day.

With the non-specific soluble antigens the complement-fixation reactions became positive at an earlier stage in most cases.

The Weil-Felix (*OX19*) reaction was positive on or before the 7th day in all of the six cases in which early tests were made. No negative reactions occurred after the 9th day. The *OX2* reaction became positive considerably later or remained negative, the titres were always much lower than those with *OX19*.

The authors state that "Differentiation of epidemic and murine typhus fever can be made by complement-fixation or rickettsia-agglutination if highly purified antigens are used."

[If this statement implies that the differentiation can always be made by either of the two tests it seems to need qualification in view of the possibility that all strains of rickettsiae causing epidemic and murine infection may not give the same reactions as the strains dealt with by the authors. The delay in appearance of the specific complement-fixing antibodies is a drawback and it seems likely that the simple rickettsia-agglutination test with purified rickettsiae will hold the field as the best routine test for use in the differential diagnosis of the typhus fevers.]

This, and the preceding paper should be read and kept for reference by every worker on the serology of the typhus fevers.

John W D Megaw

**SOMAN, D W** A Study of Weil-Felix Reaction in the Diagnosis of Typhus Fever in Bombay *Indian Med Gaz* 1947, Nov, v 82, No 11 649-53 [17 refs]

The positive reactions observed in several groups of persons tested by the Weil-Felix method are summarized in the table which has been prepared from the material supplied in the paper

Numbers of Positive Weil-Felix Reactions Observed

	<i>Proteus OX19</i>			<i>Proteus OX2</i>			<i>Proteus OXK</i>		
	1-50	1-100 to 1-250	1-500 or over	1-50	1-100 to 1-250	1-500 or over	1-50	1-100 to 1-250	1-500 or over
	1	3	0	0	0	0	1	0	0
500 sera sent for Wassermann test	5	16	28	2	2	0	2	1	1
763 sera from febrile patients including typhus cases	1	1	0	1	0	0	1	0	0
185 sera from enteric group cases	0	1	22	1	10	1	0	2	2
28 sera from typhus-group patients									

It will be seen that there is no evidence of the occurrence of anamnestic rises in the Weil-Felix titre in cases of enteric-group fevers.

In 23 of the typhus-group cases the reaction was of the *OX19* type in eight of these, guinea-pig inoculation was carried out and *Rickettsia mooseri* is said to have been isolated from two of the patients in four other cases the animals gave a febrile reaction and in two there was no reaction.

In two cases the reaction was of the *OX2* type serum from one of the patients was inoculated into a guinea-pig, with a negative result.

In three of the cases the reaction was of the *OXK* type and from each of the patients *Rickettsia orientalis* is said to have been isolated by mouse inoculation.

[The author like most other observers in India, seems to regard it as axiomatic that the occurrence of a *Proteus* OX19 type of agglutination indicates flea-borne murine typhus and excludes tick-borne typhus. PIOTZ *et al.* found that many cases of the tick-borne Rocky Mountain spotted fever gave an agglutination response of the OX19 type, and that the complement-fixation test was needed to differentiate the disease from louse-borne and flea-borne typhus (See, for example this *Bulletin*, 1945 v 42, 608.)] *John W D Meigs*

CALDERO C. Outbreak of Typhus of the Murine Type. First Report from the Isthmus of Panama. *Amer J Trop Med.* 1948, Mar v 28, No 2, 313-21 [22 refs.]

Since 1832, sporadic cases of murine typhus have been diagnosed in the Isthmus of Panama at the average rate of three each year.

Between January 15 and February 5 1947 there was an outbreak of 13 cases in the city of Panama. All the patients had worked in, or visited, a food store in which dead rats were found shortly after the occurrence of the first case. The cause of death of the rats was not ascertained.

Complement fixation and rickettsia-agglutination tests strongly supported the diagnosis of murine typhus. *John W D Meigs*

RIGHTS, F. L. & SMADEN, J. E. assisted by ELIZABETH B JACKSON. Studies on Scrub Typhus (Tsurugamushi Disease). III. Heterogeneity of Strains of *R. tsutsugamushi* as demonstrated by Cross-Vaccination Studies. *J E par Med.* 1948, Apr 1 v 87 No. 4 339-51 [28 refs.]

It has already been found that animals which have recovered from infection with one strain of *Rickettsia tsutsugamushi* (*orientalis*) are immune to all other strains of the organism although striking differences have been shown to occur in the antigenic structure of the various strains when they are tested by complement fixation, serum protection, and toxin antitoxin tests.

In the present study, the authors have found that Swiss mice inoculated with vaccines made from the tissues of rats infected with various strains of *R. tsutsugamushi* usually became protected against homologous strains but often remained susceptible to infection with certain heterologous strains. Examples of the degree of protection conferred by vaccines of different strains are shown in the table.

Strains of Vaccines	Degree of Protection Conferred against Challenging Strains				
	Imphal	Karp	Komral Mt 21	Volner	Secran- kayre (Malaya)
Imphal (India-Burma border)	++	+	+	0	0
Karp (New Guinea)	+	++	+	0	0
Komral (New Guinea)	++	-	++	0	0
Mt 21 (New Guinea)	++	+-	+	+-	0

++ means Immunity Index 2.5 or above + means Index 1.5 to 2.4  
+- means Index 0.5 to 1.4 0 means Index below 0.5



Remarkable results obtained were — (1) Vaccine made from Mite 21 strain gave little protection against infection with the same strain, but good protection against the Imphal strain, and (2) None of the four vaccines protected the mice against infection with the Seerangayee strain.

In spite of the obvious antigenic differences, the authors do not think it desirable to "indulge in taxonomic speculations regarding division of the subgenus *R tsutsugamushi*." The following comment is given in the authors' own words to illustrate the need for an agreed nomenclature of the typhus rickettsiae — "It may be noted that while cross-immunity is exhibited by animals which recover from infection with *Rickettsia prowazeki* and *R typhi*, or from infections with *Dermacentor rickettsi* and *D coroni*, nevertheless, vaccines prepared against one member of the pairs of agents afford comparatively little protection against the other" [Some readers are sure to be puzzled by the last three of these names which refer respectively to the rickettsiae of murine typhus, of Rocky Mountain spotted fever, and boutonneuse fever "*R coroni*" is, of course, a misprint for *R conori*]

JOLGOPOL, Vera B. **Histologic Changes in Rickettsialpox.** *Amer J Pathol* 1948, Jan, v 24, No 1, 119-33, 10 figs on 4 pls

A detailed description is given of the histology of the initial lesion, the maculopulo-vesicular rash, and a lymph node, as observed in biopsy material from patients suffering from rickettsialpox.

The initial lesion closely resembled the eschar of scrub typhus, both in its histology and naked-eye appearance but it was more superficial and the vascular changes were less severe. Perivascular infiltrates were seen, but plasma cells were absent and mast cells were more numerous than in the eschar of scrub typhus.

The rash was similar in its microscopical features to that of other rickettsial diseases except that the cell infiltrates were much more profuse. The vascular changes were similar to, but less severe than, those of scrub typhus. The occurrence of vesicles in the spots is regarded as a unique feature of rickettsialpox among the rickettsial diseases.

The only evidence of damage to the lymph node was the presence of mast-cell infiltration of the lymphoid tissue, there was no necrosis of the lymph node such as has been described as occurring in scrub typhus.

KOHL, G M & PARKER, R R. **Occurrence of the Brown Dog Tick in the Western States** *J Econom Entom* 1948, Feb, v 41, No 1, 102

This note records the occurrence of *Rhipicephalus sanguineus* in four additional Western States of the U S A, namely Montana, Wyoming, Utah and Nevada.

H J O D Burke-Gaffney

## YELLOW FEVER

LEVI CASTILLO R. **Historia de la fiebre amarilla selvatica en America del sur en los primeros quince años (1932-1947)** [Jungle Yellow Fever in South America in the Period 1932-1947] *Kuba* Habana 1948, Feb, v 4, No 2, 37-42 [18 refs]

[An account of much interest and useful for reference, but unfortunately not lending itself to abstract] The author traces out year by year and

from a study of the records how rural and jungle yellow fever has spread from place to place (or been discovered in one place after another) or observed more widely in various parts of South America. In the Chanaa Valley first, thence to San Ramon in Bolivia and Caparrapi in Colombia the following year to Matto Grosso next to Ecuador and much of São Paulo and other States, Minas Gerais, Paraná, Espírito Santo.

[Many of the references given are to papers and articles already abstracted in this *Bulletin* and others have been abstracted to which the author does not refer]

H. Harold Scott

## PLAGUE

WYNN-GRIFFITH, G. Pneumonic Plague in Rangoon. *Lancet*. 1948, Apr. 4, 625-7. [25 refs.]

In Burma plague has long been endemic, and the same of course applies to Rangoon. Rangoon, however has no record of a series of cases of pneumonic plague such as the present outbreak. It occurred in September and succeeded an earlier bubonic epidemic in spring. There were 18 deaths, but suspicion of the nature of the disease did not arise until the occurrence of case 11 which was the first notification to the health authorities. The epidemic had much the same course as other epidemics and much the same nature—high fatality rate and highly restricted area of diffusion. The epidemic rapidly burned itself out. An interesting point is raised in discussion—the assumption that pneumonic plague is very infectious. That assumption is questioned and, certainly in the present epidemic, the conclusion might be reached that “the disease is not particularly infectious.” Preventive measures are rightly to be taken in spite of the fact that “theoretically pneumonic plague is easily controlled.” The author continues—“The incubation period is relatively short—hence very few contacts will become cases after a week’s quarantine. There is a distinct non-infectious phase lasting twenty-four to forty-eight hours after the onset of clinical illness. Immediate isolation during this phase of all cases of suspicious illness will effectively abort the outbreak.”

H. F. Harvey

See also p. 708 TORCHIE, Neuere Erfahrungen und Bestrebungen bei Cholera- und Pestimpfungen.

## CHOLERA

KHALLI Bey M. The Defence of Egypt against Cholera in the Past, Present and Future. *J. Roy. Egyptian Med. Soc.* 1947 Dec. v. 30 No. 1, 608-55. [12 refs.]

This address, which was delivered on 31st October 1947 was doubtless given to a special audience. It has particular interest at the present time as forecasting a possible or probable appearance in May 1948 of the epidemic of cholera which has ravaged Egypt anew after a long interval of freedom. For the prevention of this danger much evidently depends on the public health authorities. There are many details of historical interest set out very emphatically. Even more important than the views expressed as to the origin of the present epidemic, which follow current lines, is the declaration that reform is needed in the public health administration and the quarantine

administration of Egypt The Egyptian Government has acted vigorously in providing funds for hygienic necessities There is obvious need to provide a pure water supply from tube wells to three-quarters of the Egyptian villages, and the experience of the value of such a supply has been amply demonstrated in the present epidemic by the comparative immunity from cholera of urban populations provided with an urban type of water supply

The old questions of the danger of the Mecca pilgrimage for Egypt according to the time of year at which it takes place are discussed Evidently the institution of the quarantine station of El Tor has justified itself It is now necessary with air travel, to have a new convention to replace that of 1944, for the protection of Egypt is considered to be equivalent to the protection of Europe

RAYNAL J H Quelques mots sur le choléra en Egypte (automne 1947) [A Note on the 1947 Cholera Epidemic in Egypt] *Méd Trop* Marseilles 1947 Nov-Dec v 7 No 3 470-74 1 chart & 1 map W F Harvey

KHALIL Bey M The Effect of the Absolute Humidity of the Atmosphere on the First Wave of the Cholera Epidemic in Egypt in 1947 *J Roy Egyptian Med Ass* 1948, Jan v 31 No 1, 39-72 9 charts & 1 map

GOHAR, M A & MAKKAWI, M Some Observations on the Cholera Vibrio Isolated from the 1947 Egyptian Epidemic *J Roy Egyptian Med Ass* 1947, Nov, v 30, No 11, 525-9

"1 The morphology, cultural characters, resistance and pathogenicity of the Korain strain of cholera vibrio correspond to a large extent to those of the classical strains, except perhaps that the vibrio is not very markedly curved and rather short

"2 Serologically it was found identical with the Inaba strain which is known to be the most prevalent strain in certain parts of India

"3 Its short life inside dates is apparently due to the acidity produced by the fermentation of the carbohydrates present abundantly in them Ten per cent lemon juice is enough to kill it almost instantaneously "

GOHAR, M A & MAKKAWI, M Potassium Tellurite in the Isolation of the Cholera Vibrio *J Roy Egyptian Med Ass* 1947, Nov, v 30, No 11, 556-61

The common enrichment method of isolation of the cholera vibrio by inoculation of stools in alkaline peptone water, incubation for 6 to 8 hours and then plating on alkaline agar may delay the isolation, or even render it more difficult than direct plating Several experiments were undertaken to determine the meaning of this in terms of antibacterial action or overgrowth by other organisms, such as *Bact alkaligenes*, *Bact coli* and enterococcus Antibacterial action was disproved and overgrowth incriminated In fact the suggestion is made that it is the possession of an intestinal flora with the power of overgrowth that may determine infectivity for the individual

The main endeavour was to find a selective bacteriostatic substance to incorporate in the nutrient medium, which would inhibit the growth of *Bact alkaligenes* and *Bact coli*, with less or no effect on the cholera vibrio The substances tried were potassium tellurite potassium and sodium selenite mercurochrome, methylene blue, thionin, basic fuchsin, brilliant green, crystal violet, neutral red, eosin and flavin Of these, potassium tellurite proved the best when added to alkaline peptone water in a dilution as great as of 1 in 50,000 This has little effect on the cholera vibrio and the enterococcus, but has

bacteriostatic action on the other organisms. The enterococcus gave little trouble in the isolation of the cholera vibrio. Thus this method of enrichment "is recommended for the examination of convalescents, contacts, water and other suspected materials."

W. F. Harvey

GOMAR, M. A. & MARKAWI, M. Cholera in Egypt. Laboratory Diagnosis and Protective Inoculation. *J Trop Med & Hyg* 1948, May v 51 No. 5 95-9

One or two points regarding the recent outbreak of cholera in Egypt are brought out in this and the several papers which have appeared on the subject. It "created a state of terror almost amounting to panic." The authors have devised a valuable method for reducing labour and saving time in the laboratory by illuminating the contaminating overgrowth of the "true cholera vibrio by *Bact. alkaligenes*. This method has been described above (see also this Bulletin 1948 v 45 600) and depends on the motility of the vibrio, its aerobic character and the inhibitive action of potassium tellurite. The "true cholera vibrio is truly a highly selected organism.

A feat in mass vaccination was accomplished. General vaccination of a population amounting to nearly 20 million people was achieved in Egypt probably for the first time in the history of this disease. One dose of 8,000 million organisms was given to everybody—very few people received 2 doses. As bacteriologists, the authors are cautious in their deductions. It would be rash to try and draw any conclusion as to the value of general vaccination adopted in this epidemic.

An extensive research was conducted into the viability of the cholera vibrio on various articles of food and clothing. A high correlation between the time of collection of cases and the time of occurrence of a cholera epidemic is commented on.

W. F. Harvey

GOMAR, M. A. A Rapid Method for the Bacteriological Diagnosis of Cholera. *J Roy Egypt Med Ass* 1947 Nov 30, No. 11 555-558 fig

[See this Bulletin 1948 45 600]

TAKAMAI, S. J. W. Een Serologische en een colloïd-chemische reactie ter onderscheiding van cholera en El Tor vibriën. [A Serological and Colloïd-chemical Reaction for Cholera and El Tor Vibrios.] *Nederl. Tijdschr v Geneesk* 1948 May 8 92 (1) No 19 1570-75 English summary

With the discovery of an El Tor vibrio strain in Celebes the El Tor question as the author says, was infused with new life. Regulation tests for the true cholera vibrio were reviewed: haemolysin production—a bad guide—not an production—unsuitable in practice; acetylmethylcarbanol formation—no differential value; serum reactions—not distinctive. He is speaking, especially of the differentiation of the haemolytic El Tor vibrio from the true cholera vibrio and of antigenic analysis. This leads up to his introduction of a colloïd-chemical test. A serum reaction is regarded as occurring in two phases: the first of fixation of antibody or sensitization and the second of flocculation by sodium chloride or saline as electrolyte. He has used as serum the Damang O-antiserum which is probably identical with the Hikojima or intermediate type. A number of electrolytes were tested and of these sodium carbonate  $\text{Na}_2\text{CO}_3 \cdot 10\text{H}_2\text{O}$  was the most suitable while sodium bicarbonate was unsuitable. In this test a high-titre disinfectant free cholera antiserum was diluted 1 in 200 with 0.3 per cent sodium carbonate, and to it was added a concentrated vibrio

suspension in distilled water. The mixture is well shaken and it should be found that cholera vibrios remain consistently inagglutinable while El Tor vibrios flocculate completely and are deposited. If the soda solution is set up in series 0.1, 0.2, 0.3, 1.0, 2.0, 5.0 per cent, it is found that up to 0.2 per cent both vibrios flocculate out, above 0.2 per cent only El Tor still flocculates, but above 0.5 per cent the El Tor also remains in consistently stable suspension.

The second test depends on the replacement of the serum by chemical solutions alone. A few drops of concentrated vibrio suspension in distilled water are added now to the solution previously found unsuitable, namely, a 0.5 per cent  $\text{NaHCO}_3$ , and after 15 minutes an equal volume of 0.5 per cent mercuric chloride is added to the mixture. Now the phenomenon is reversed: cholera vibrios flocculate immediately, while El Tor vibrios remain in uniform suspension.

W F Harvey

GREPPIN, J. Mission médicale suisse en Egypte [Swiss Medical Mission in Egypt] *Bull. Internat. Services de Santé des Armées* Liège 1948, Mar-Apr, v 21, Nos 3/4, 53-61.

Switzerland through its Red Cross organization acted swiftly and philanthropically in offering its help to the Egyptian Red Crescent to control the outbreak of epidemic cholera. The offer was gratefully accepted and the party of doctors, technicians and hospital sister got to work at the small 25-bed hospital of Kafr-el-Zayat in the Delta region between Cairo and Alexandria. They found 186 patients in the hospital area. Patients commonly arrived comatose, dehydrated and cold. Treatment for shock consisted of the administration intravenously of 5 to 10 litres of glucose-saline in the 24 hours. Hypertonic saline or bicarbonate of soda solution were required for acidosis, while hypoproteinaemic patients received infusions of plasma.

The average case-mortality rate in this hospital has been calculated at 30 per cent, contrasting with that of Egypt generally, which was 50 per cent.

A laboratory was attached to the hospital, and although equipment was short much good work was done in isolating vibrios. A very active cholera phage was isolated, which caused lysis in the high dilution of  $10^{-10}$  and was used to differentiate the Egyptian cholera strains from the El Tor vibrio and non-pathogenic strains.

Three villages and the population of Kafr-el-Zayat were treated with DDT, of which the Swiss had 1,000 kgm of 50 per cent powder. This was used in 2 per cent aqueous suspension (1 per cent of the active ingredient) for the walls of houses and sprayed by motor pumps under pressure of 20 atmospheres. Its lethal effect was observed not only on flies, but on lice, fleas, bugs, cockroaches, wasps and mosquitoes. The anticholera mission returned to Switzerland on 17th December.

W F Harvey

HALAWANI, A. & OMAR, A. A. Effect of Copper Sulphate on *Vibrio cholerae*. *J. Roy. Egyptian Med. Ass.* 1947, Nov, v 30, No 11, 547-52.

'1 Copper sulphate is lethal in dilutions ranging from 20-45 parts per million to *Vibrio cholerae* in concentrations ranging from 10 to 1,000 million per cc of Nile water.

"2 We believe that copper sulphate has its place in the prevention of cholera especially as it is used in this country in the eradication of snails in water canals."

sub-inoculation of the guineapig's blood or brain into a rat or mouse. The tick-borne spirochaetes vary in their receptivity to the guineapig. *Sp. hispanica* (sic) of North Africa always produces a patent infection. The South American strains—*Sp. [Trep.] recurrentis* and *Sp. [Trep.] neotomae*—are completely refractory. It is concluded that the susceptibility of the guineapig provides a good biological test. [This test would be of little value in tropical Africa, where the reviewer and his co-workers (this *Bulletin* 1948, v 45 88) showed that both types of spirochaetes were occasionally able to infect guineapigs. A better method of differentiating these African strains is to observe their behaviour (a) in monkeys (*fatalis* is fatal, *recurrentis* is not) and (b) in mice (*fatalis* causes persistent infections, *recurrentis* lasts for 7 or 8 days only).]

P. C. C. Garnham

CONSTANTINESCU G. & JONESCU R. Contribuţiuni la studiul forme meningeale în febra recurentă. [Observations on the Meningeal Form of Relapsing Fever.] *Rev. Stiintific Med. Bucurest.* 1947 Nov-Dec., v 36 No. 11/12, 503-8. French summary (4 lines)

Of 285 cases of relapsing fever studied in 1945 12 were of a meningitic type. The cerebrospinal fluid was usually clear and not under pressure, and sometimes showed xanthochromia or gross haemorrhage. In no case could the causative organism be demonstrated in the cerebrospinal fluid. Meningeal signs appeared at the first onset of fever. They cleared up during the apyrexial period and did not reappear during the next onset of fever. The nervous symptoms were unaffected by arsenical treatment.

D. J. B. Carr

## YAWS

DILLON M. L. & COOPER, G. R. Electrophoretic Analysis of Serum from Patients with Pinta and Yaws. *Am. J. Syph.* 1948, May, v 32, No. 3 231-5 1 fig. (18 refs.)

"The electrophoretic analyses of three pinta and three yaws sera revealed a slightly increased content of  $\gamma$  globulin in the pinta sera and a larger increase in the  $\gamma$  globulin fraction of the yaws sera. The albumin content was proportionately low in comparison with the  $\gamma$  globulin content. No specific changes in the electrophoretic patterns indicative of the presence of unique proteins appeared in the diagrams of the pinta and yaws sera."

YAMBEI SEGHEM, R. *Planities pocrisiformes*. *Acta Tropica* Nankai. 1947 v 4 No. 4, 353-4, 2 figs.

Report of a case in an African girl of 10.

## LEPROSY

MUIR, E , KIRWAN, E W O G ADAMS, A R D Symposium on Leprosy- Recent Advances in the Treatment of Leprosy [MUIR] *Trans Roy Soc Trop Med & Hyg* 1948, Mar, v 41, No 5, 575-82 The Eye in Leprosy [KIRWAN] *Ibid* 583-90, 2 coloured figs on pl [16 refs.] Three Cases of Leprosy treated with Diasone [ADAMS] *Ibid* 591-4 Discussion 595-9 [MANSON-BAHR, P MAC ARTHUR, W , COOKE, W E BROWNLEE G , CHESTERMAN C C , GRAY W H , MUIR, E , KIRWAN, E W O G ; ADAMS, A R D]

The opener of this discussion dealt almost entirely with trials of the new sulphone drugs, promin, diasone, promizole and sulphetrone of Burroughs Wellcome & Co on the lines of his earlier papers on the first two arrest of the disease may be expected in the majority of lepromatous cases in about five years Promizole was found less effective by U S A workers and has been given up by them, as it is difficult to make, expensive and it presents no advantages except that it is slightly less toxic than some Of greater interest is the statement that early reports on the use of sulphetrone indicate that it is less toxic and gives quicker results than the other sulphones yet tried All of them require hospital treatment to enable resulting anaemia to be detected and treated with iron and liver preparations, to which Muir advises the addition of vitamin B in the form of yeast In patients subject to reactions, small doses should first be given, such as 0.3 gm of diasone or 0.5 gm of sulphetrone, both orally every other day, cautiously increased to 2 gm on alternate days This point may be reached in a few weeks or it may take many months In early uncomplicated cases the dosage may be increased more rapidly A fall of haemoglobin below 70 per cent is an indication to stop the drug, as is the occurrence of reactions. Destructive effects of sulphones on lepra bacilli are only well marked in the neighbourhood of capillary blood vessels DAVEY has recently reported from Nigeria some lepromatous cases in which the lepromin test has changed from negative to positive within 5 to 10 months under sulphetrone Tuberculoid cases, with few lepra bacilli, do not apparently respond as well to sulphones. Improvement occurs in most lepromatous cases in 2 or 3 years Greatly increased accommodation and medical staff in resident institutions will be necessary to enable the prolonged sulphone treatment to be carried out in all lepromatous cases, but with the promise in time of greatly reduced numbers of highly infective cases

KIRWAN spoke on eye infections in leprosy from a large experience in Madras and gave a table of their frequency varying from 42 to 100 per cent They occur in neural cases as a result of the exposure of the cornea owing to muscular paralysis, and in lepromatous cases owing to infection through the blood stream The original paper should be consulted for detailed description Treatment is difficult, but penicillin is advised locally for conjunctivitis The slit lamp with the corneal microscope and the electric ophthalmoscope are essential for diagnosis

ADAMS reported three lepromatous cases treated with diasone with marked retrogression of the skin lesions but no obvious diminution of the bacilli MACARTHUR spoke on misconceptions regarding the incidence of leprosy during Biblical and mediaeval times due to too literal interpretations of words which in early times had a wider and more general application than they now have

BROWNLEE spoke on the toxic effects of sulphones and described the resulting anaemia as hypochromic at first, but later of the nutritional type The latter

he attributes to a change in the intestinal flora which cuts down the biosynthesis of vitamins of the B-complex group. Yeast treatment is indicated in such cases.  
L. Rogers

AYCOCK, W. L. A Proposed Study of Conjugal Leprosy with reference to Contagion and Hereditary Susceptibility. *Internat. J. Leprosy* 1948, Jan.-Mar. v 16 No. 1 1-8, 2 charts.

This paper discusses the possible light thrown by the incidence of conjugal infections on the difficult question of the relative influences of contagion and hereditary susceptibility. The following are the main points in a largely theoretical discussion. The occurrence of several cases in one family may be due to either contagion or heredity. The infection of twice as many males as females is more in keeping with the Mendelian operation of hereditary susceptibility. Data on conjugal leprosy might help to decide between susceptibility and prolonged exposure to contagion, but age susceptibility complicates the question. The rarity of conjugal leprosy allows of comparative studies of regional, racial and familial factors. More frequent child infections may be due to greater exposure to infection. Consideration of both the interval after conjugal exposure and the age at which the disease occurs would make it possible to distinguish between prolonged exposure and familial susceptibility as the probable determinant in conjugal infection. Reference is made to a previous paper by the author and Gordon (*this Bulletin* 1948, v 45 186) on leprosy in veterans of American wars, which showed that Spanish American War veterans from non-leprosy regions acquired their initial exposure on military service. In World Wars I and II veterans from foci of the disease were found to be infected during or shortly after their military service and developed their disease within a few years of beginning their service, whereas Spanish War veterans developed theirs on an average of 23 years after their military service and at an age 20 years later than the former. It is therefore anticipated that conjugal cases may show a similar pattern of two groups of development of the disease, either soon after marriage or at a much longer interval, and at later ages. The latter are likely to have contracted the disease from their spouses, the former through previous exposure in their own families. Further studies of conjugal cases on these lines are indicated. A suggested table for notes on cases of conjugal leprosy is given.  
L. Rogers

SEAR, P. A Plan for the Study of Social Aspects of Leprosy. *Leprosy in India* 1947 Oct., v 19 No. 4 123-7

DE SOUZA-ARAÚJO, H. C. Descoberta isolamento de um bacilo ácido-alcoól resistente de cartapato ("Amblyomma rotundatum") capturado em sapo ("Bufo marinus"). "Mycobacterium lateri" n. sp. Nota póstuma. [Isolation of an Acid-Fast Bacillus from a Tick (*Amblyomma rotundatum*) captured on a Toad (*Bufo marinus*). *Mycobacterium lateri* n. sp.] *Brasil-Médica* 1948, Jan. 17 4 & 31, v 62, Nos. 3, 4 & 5, 17-19, 2 figs. English abstract 18-19.

DE SOUZA LIMA, L. & DE SOUZA CAMPOS, N. Immune-Biology Abnormalities in Leprosy. *Internat. J. Leprosy* 1948, Jan. Mar., v 16 No. 1 9-22.

In this important paper Mitsuda, or leproskin, reactions on 601 patients in 1941 are tabulated under the types of "uncharacteristic" and tuberculous and the subsequent variations in the reactions and the evolution of the cases are examined. The sixteen tables should be studied in the original, but the following are the conclusions arrived at. Of 216 uncharacteristic cases 60 were



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*Leprosy*

negative in 1941, 41, or 68.3 per cent, of which had developed into the lepromatous type by 1946. Of 139 positive cases, 33 or 23.7 per cent, became lepromatous. A much smaller proportion of strongly positive (3 plus) became lepromatous than of weak (1 plus) cases. Nevertheless, the general assumption regarding the prognostic value of the test is by no means universal. Among 685 tuberculoid cases 592, or 86.4 per cent, gave positive reactions, 79, or 11.5 per cent, negative and 14, or 2 per cent, doubtful reactions. Only 17, or 2.9 per cent, of the positive cases developed into the lepromatous type, but of the negative cases 29, or 36.7 per cent, became lepromatous, together with 1 of the 2 doubtfully reacting ones. The prognostic indications of the test were thus more accurate in the tuberculoid cases, but not absolute. In some cases of both types a change occurred from a positive to a negative type and *vice versa*. In 3 of the latter, the lepromatous type nevertheless developed, among those changing from positive to negative, lepromatous transformation occurred in all except one patient.

L Rogers

Box, Louise A. **Benadryl in Acute Lepra Reactions.** *Hawaii Med J* 1948, Mar-Apr, v 7, No 4, 303-4

The author reports on a trial of an anti-histamine drug, Benadryl (B dimethylaminoethyl benzhydryl ether hydrochloride) in the allergic reactions of leprosy. The 9 treated cases include 3 with acute lepra reactions of spontaneous occurrence, 4 with acute lepra reactions apparently precipitated by promin treatment, and two with "major tuberculoid" reactions. The effects were compared with histories of previous reactions, of which it was not always possible to get reliable accounts. An average dose of 50 mgm is given three times a day and continued from a few days to several weeks in accordance with the length of the reaction. The three spontaneous acute reactions appeared to respond well, as did the four which had followed promin treatment, but the two major tuberculoid ones gave equivocal results. The patients had no pain and no new lesions developed during a reaction. The author is cautious in coming to conclusions, but thinks further investigation of anti-allergic drugs in the treatment of acute leprosy reactions is indicated.

L Rogers

CHANDY, P J. **Iodised Hydnocarpus Oil in the Treatment of Leprosy** *Leprosy in India* 1947, July, v 19, No 3, 72-9

The author reports on the treatment of 44 cases, most of which were lepromatous and bacteriologically positive, by iodized hydnocarpus oil prepared by the following method so as not to contain any free iodine. 36 grams of re-sublimed iodine are dissolved in 1 ounce of ethyl ester of hydnocarpus oil, this iodine ester is then poured into a one pound bottle containing 15 ounces of hydnocarpus oil. The contents are well shaken and the whole is then sterilized in an autoclave at 15 lb pressure for half an hour. Heat-proof glass bottles should be used. Injections are free from pain and as much as 10 cc can be injected intramuscularly at one site without induration or other trouble and without serious reactions. The injections were given once a week for two years, to a total amount of over 400 cc. Nodules flattened and in time disappeared, bacilli decreased and the majority of the cases became bacteriologically negative, especially those in which the organisms were not very numerous at first. The results were better than with Hydnocroal. A table shows details of the cases.

L Rogers

E

DEARMENDRA & SEN V. Erythrocyte Sedimentation Test not necessary for regulating Treatment with *Hydnocarpus* Balmolies. *Leprosy in India*. 1947 Oct. v 19 No. 4 123-30 6 charts on 1 folding pl.

"For regulating the dose of the *hydnocarpus* oil it is not necessary to take into consideration the results of the sedimentation index. The treatment can very well be regulated by the clinical condition of the patient. The sedimentation index does not provide any additional information."

DE SOUZA LIMA, L. Tratamiento experimental de la lepra. (The Treatment of Leprosy) *Medicina*. Mexico. 1948 Mar 25 v 28, No. 552, 129-33.

The reason for calling this treatment experimental is not quite clear. The author states that *chanbmoogra* has a false reputation and that he has no belief in its efficacy for three reasons: 1. That good report of its use has been (in the Padre Bento Sanatorium) in tuberculous forms, yet in about 98 per cent. of 200 cases this disease retrogressed spontaneously and the remainder progressed even to mutilation in spite of the treatment. 2. That observation over 4 years of "two lots" (the numbers of patients are not given) of non-characteristic forms of leprosy one group receiving *chanbmoogra*, the other not showed that the same percentages were transformed into lepromatous, or tuberculous, or retrogressed in each group, so that the painful treatment with *chanbmoogra* had no effect and might just as well have been omitted. 3. That *chanbmoogra* did not influence the progress in a thousand cases under observation (those of the lepromatous form which seemed for a time to improve relapsed again within a comparatively short period. *Chanbmoogra* preparations were given intramuscularly or intradermally in varied doses.

The author then relates his experiences with Promin, given intravenously each day, starting with 1 cc. and increasing gradually to 5 cc. administration being for a fortnight, followed by a week's remission. Next, with *Diasone* given orally in doses of 0.33 ggm. (0.33 gm.?) daily for 6 weeks, followed by a rest for a fortnight. From these singly or combined, excellent results are recorded, even in cases of ocular leprosy. In ordinary cases infiltration was reduced, discoloration gave place to a normal skin, and biopsy search for bacilli showed steady reduction. At first *Diasone* seemed to aggravate the skin conditions, infiltrations became more swollen, lesions extended and fresh ones appeared, but they soon cleared up if the treatment was persisted with.

H. Harold Scott

DAVISON, A. R. Antimony in the Treatment of Leprosy. *Internat. J. Leprosy* 1948 Jan. Mar., v 16, No. 1 23-8, 13 figs. on 2 pls.

Experience at the Pretoria Leper Institution supports the view that antimony has the power of controlling lepra reactions and benefit erythema nodosum leproticum. Insulin is also being used, but the author has not yet decided which is the better treatment. The drug is also of value in tuberculous cases in the re-active phase and in neural cases which are developing new macules through having a lowered resistance. Fouladin is given in courses of ten intramuscular injections followed by a fortnight without treatment. Continued and intensive courses of antimony treatment were not beneficial. If antimony fails to build up resistance leumuth may be of value. The appearance of new lesions is an indication for stopping *chanbmoogra* treatment. Most of the cases were of the neural type but in three lepromatous cases antimony helped to render them free from bacilli. Antimony may also be of

use as an adjuvant to promin treatment Antimony is not a specific cure for leprosy, as failures have equalled the successes, and the treatment must be adjusted to every individual  
L Rogers

GASS H H The Use of Massage in Leprosy *Leprosy in India* 1947 July v 19, No 3 80

AUSTIN, C J Central Leper Hospital, Makogal (Annual Report 1946) *Fiji, Legislative Council Council Paper No 1* 1948, Appendix 7, 20-27 1 diagram.

MASIH, M Leprosy and Anti-Leprosy Work in Almora. *Leprosy in India* 1947, July, v 19 No 3 81-5, 2 maps

### HELMINTHIASIS

DE MEILLON, B Aspects of the Natural History of Bilharzia in South Africa. *South African Med J* 1948, Apr 10 v 22 No 7, 253-60 1 map [16 refs]

An account of this paper, which was read at a medical congress at East London, has been reviewed in this *Bulletin* 1948, v 45, 190

See also p 671, HEISCH, A Parasitological Survey of Taveta

ERFAN, M & TALAAT, S Demonstration of *Schistosoma* Ova in the Liver by Biopsy *J Roy Egyptian Med Ass* 1947, Dec, v 30, No 12, 663-4

The authors obtained liver biopsies in 41 cases of Egyptian splenomegaly. The biopsy was carried out under local anaesthesia by means of a small-calibre lumbar puncture needle, the tip of which is "debevelled to act as a trocar and cannula". The instrument is pushed 2 to 3 cm into the liver during full expiration, the trocar is withdrawn and a 10 cc Record syringe fitted tightly to the cannula. Suction is applied, the cannula is pushed in another 2 to 4 mm and withdrawn while suction is maintained. The puncture is sealed with collodion. The preliminary anaesthesia is obtained by infiltration of the skin, the pleura and peritoneal covering of the liver with a total of 10 cc of 2 per cent novocain solution.

The liver substance obtained is washed in saline and digested in a centrifuge tube with 5 drops of 4 per cent sodium hydroxide, the tube is warmed until digestion is complete, when the material is centrifuged and examined for ova.

Schistosome ova were found in 21 cases. 11 were *S. mansoni*, 5 were *S. haematobium* and in 5 cases, ova of both species were found. In 4 cases, *S. haematobium* ova only were found in both liver and faeces specimens. In 7 of the 21 cases, faecal examinations were negative, but ova were found in the liver.

Ova were present in liver, faeces or urine in 39 of the 41 cases, which the authors state "practically disposes of the theory that hepatic bilharziasis is due to infection with male schistosomes".

In 19 of the positive cases having ova in the stools, the liver and spleen were enlarged.

In one case, ova were present in the liver although neither it nor the spleen was enlarged.

It is concluded that liver biopsy is a simple, safe and useful means of diagnosing hepatic schistosomiasis.

H J O'D Burke-Gaffney

LOVERIDGE F G, ROWS W F & BLAIR, D M. Schistosomiasis: the Effect of the Disease on Educational Attainment. *South African Med J* 1948, Apr 10 & 22, No. 7 260-63.

KISSER [this *Bulletin* 1948 & 45 526] observed the deleterious effect of urinary schistosomiasis on the scholastic attainment of children in Transvaal schools. In Southern Rhodesia, school teachers in European Schools frequently suspect schistosomiasis as an explanation of forgetfulness and lack of concentration in some of their pupils, and it is striking how often this tentative diagnosis is confirmed by medical examination and parasitological investigation.

In the case of European children tests were made in two boys' schools which were generally comparable except that one gave an academic and the other a modern education. In general, the average intellectual standard was higher in the former.

"Presumptive" infections were diagnosed by a cercarial antigen skin test and proved infections were those afterwards confirmed by the finding of ova in the urine or stools or both.

A table indicates that in both presumptive and "proved" infections the schistosomiasis rate was significantly higher in the boys from the modern school the findings being 74 and 27 respectively from 91 boys, compared with 37 and 9 from 118 boys in the academic school. The statistical significance of these figures is shown.

In the case of African schoolchildren, an investigation was carried out on 365 pupils of both sexes in one school—those in 11 classes were grouped on school examination results into upper and lower halves in each class—a note was made of those who failed in the examination. The results are shown in a table from which it emerges that the "proved" infection rate averaged 50 per cent. Nevertheless, these did not represent the main constituent of the lower half of each class—indeed the infected children made a slightly better showing in "presumptive" and "proved" infections alike. For example, only 30 per cent. of the pupils were regarded as being uninfected on the "presumptive" criterion yet more than half of them were in the lower halves of the classes. Again, only 44 of 82 pupils who failed in their examinations had schistosomiasis. On the other hand pupils with proved infections took 43 out of the 44 places comprised by the first four places in each of the 11 classes. An additional 9 members of this group gave presumptive evidence of infection, so that some evidence of schistosomiasis was present in 77 per cent. of the pupils who won all the top four places.

It appears that schistosomiasis had no adverse effect on the educational attainment of these African schoolchildren and, indeed, the infected children seemed to fare better than the uninfected.

While admitting that the reason for this difference between the European and African children is not clear the authors observe that the African child is exposed to schistosomiasis earlier in life than the European and that the disease is more chronic in him at school age. It also may be that one more helminth infection, added to an organism already perhaps overburdened with other parasitic or nutritional influences may make little difference to the general lowering of the level of scholastic attainment—but this does not explain the better performance actually observed in the infected children.

H J O'D Burke-Gaffney

FACIST E C. An Inquiry into the Ectopic Lesions in Schistosomiasis. *Amer J Trop Med* 1948, Mar 28, No 2, 15-49 1 fig. (64 refs.)

Ectopic schistosomal lesions have been reported with increasing frequency during recent years. Many among the American and Australian troops

engaged in the highly endemic schistosomiasis areas in the Philippine Islands acquired schistosomiasis, and among these ectopic lesions have been not uncommon. The subject is therefore one of current as well as of practical importance. In this paper the literature on the subject is reviewed in some detail, and the mode of origin of the ectopic lesions is critically examined. The author gives the following summary and conclusions, but the original should be consulted by those interested.

"1 Ectopic lesions in schistosomiasis are defined as those produced by immature or mature stages of schistosomes outside the portal-caval venous blood channels with their extension into the pulmonary arterioles. The lesions occasioned by the migration of young worms have been studied critically in experimental hosts but are not histologically described for man.

"2 Interpretation of the lesions produced by schistosomes in man or other definitive hosts requires background information on the usual route of migration of the larvae from the site of their entry into the body to their arrival in the intrahepatic portal vessel, the growth of the worms in this location, their subsequent passage against the venous blood current to the mesenteric venous radicles or vesical plexus where they mature and oviposition takes place, and finally the local and systemic tissue reactions to the presence of the worms in the body.

"3 Tabulation of published and other case histories of ectopic schistosomiasis, based on autopsy, biopsy, surgical intervention and substantial clinical data indicates that there are not less than 82 known cases with 86 separate sites where these lesions have been located. Twenty-one cases with 23 lesion sites are attributed to *Schistosoma haematobium*, 12 cases with 12 lesion sites, to *S. mansoni*, and 49 cases with 51 lesion sites, to *S. japonicum*. A majority of reported ectopic lesions in *S. haematobium* infection have occurred outside the brain and its blood vessels, a significant preponderance of those in *S. japonicum* infection have been in the brain, while those in *S. mansoni* infection are too few to show any significant anatomical predilection.

"4 The tissue reaction to schistosome eggs which escape from blood vessels into perivascular tissues is an acute inflammatory one in which histiocytes, epithelioid cells, giant cells, eosinophils, plasma cells and fibrocytes attempt to wall off the invading foreign body, with the eventual production of a pseudo-tubercle around each egg as a center. Nest [*sic*] of eggs were typically found within relatively circumscribed areas, so that each lesion consists of an aggregate of pseudo-tubercles forming a granuloma that varies in size from a pinhead to an orange. The smallest ectopic lesions have been found in the conjunctivae, the largest ones have occurred in the brain.

"5 From the time of entry of the metacercariae of the human schistosomes into the cutaneous venules, following exposure to infection, the worms are characteristically intravascular in their location. There are several records of ectopic location of the adult worms, one in the middle cerebral vein, one in the ophthalmic vein, one in a coronary artery, and larger numbers from gastric, splenic esophageal, hepatic and renal veins of heavily infected experimental animals. In no instance is there any evidence of local tissue reaction to the presence of the worms.

"6 Five separate theories have been adduced to account for ectopic lesions in schistosomiasis. (1) Metacercariae develop to adult worms, with subsequent oviposition, at or near the sites of penetration into the skin or mucous membrane, (2) a patent foramen ovale would provide a direct route from the inferior caval veins into the systemic circulation, (3) eggs may escape through the pulmonary capillaries and be deposited in distant arterioles, (4) adult worms may travel against venous blood flow into collateral vessels and on reaching the end venules deposit their eggs, and (5) the vertebral

One patient with a haemoglobin of 35 per cent. died and the reader is left to assume that one of their criteria of fitness for treatment, i.e. a minimum haemoglobin level of 50 per cent., was instituted after this mishap.

In successive paragraphs, they say (1) "It is also known that the drug is excreted in 2-3 days through the kidneys" and (7) "With the standard methods of treatment the drug remains in the body for a month on an average."

Five charts are given intended to show the number of days taken to produce ova free urine but it is impossible to correlate the numbers given in the text with those given in some of the charts. Nevertheless, their two-day course is worthy of extended trial and should be very valuable in hospital work.]

W. AHERN

SAID EL AYADI M. Treatment of Bilharzia by the Oral Route. *J. Roy. Egypt. Med. Ass.* 1947 Vol., 30 No. 11 562-6.

Ten million of the population in Egypt suffer from chronic schistosomiasis. Parenterally administered trivalent antimony is unsuitable for mass treatment of the population for this infection. Methods of treatment with antimony by the oral route were investigated, attention being directed particularly to the avoidance of emesis, to the promotion of absorption of the drug from the intestine and to the establishment of the effective dosage of the selected compound.

Repodral (Fouadin) in 6.3 per cent solution was selected for trial. Tolerance to its administration by the oral route was found to be increased by giving the drug in small amounts at intervals of  $\frac{1}{2}$  to 3 hours on an empty stomach. Beginning with 4.5 ml., divided into 5 doses during the first day the amount was increased daily until on the 6th day 8.2 ml. were given the gross dosage in this period was 40.0 ml. There was no vomiting as a result of the treatment. (The number and the weight of the persons used in this experiment are not stated.)

Of the substances (unspecified) examined to promote absorption of antimony from the gut riboflavin in doses of  $\frac{1}{2}$  to 3 mgm. was found "to produce the desired effect." Its action is likened to that of vitamin D on calcium, and vitamin C on iron, absorption.

Dogs were injected with a total of 0.4 ml. of Repodral per kgm. of body weight as described by HALAWANI and ABDALLAH (this *Bulletin* 1947 v 44 230). On examination 24 hours after the last injection, the antimony content of the liver was found to be about 3.5 mgm. per cent. This amount of antimony is (assumed by the authors to be) that in human livers found by the above-mentioned workers to be lethal to schistosomes in 17 of their 15 patients. The oral dosage necessary to produce this level of antimony in the livers of dogs was 7 ml. per kgm. body weight.

Four *Cercopithecus griseo-mixtus* u. *griseoauratus* were infected with *Schistosoma haematobium* eggs appeared in their stools after 84 days. Two of the monkeys were treated with riboflavin and Repodral (2 ml. per kgm. divided into 6 doses over three successive days). A third monkey was treated with 0.6 ml. per kgm. for two doses only. The fourth was untreated.

The number of ova in the stools of the three treated monkeys gradually decreased over a period of a month the proportion of dead ova steadily increased, until after 10 to 15 days no living and only an occasional dead ova was found. After 23 days no more ova were found in the two fully treated monkeys there were scanty living ova from the incompletely treated monkey the control still produced living ova. The incompletely treated monkey was then given 0.34 ml. per kgm. of Repodral no ova were subsequently

ound over one week's daily observation. It is concluded that oral treatment of schistosomiasis with 2 ml Repodral per kgm of body weight, with riboflavin, is curative. 0.66 ml per kgm is not curative, 1 ml per kgm may be so.

A R D Adams

HALAWANI, A, NEWSOME, J & WOOTTON, I D P. Miracil D. Investigation of Blood Levels after a Single Dose. *J Roy Egyptian Med Ass* 1947, Dec, v 30, No 12, 656-62, 2 figs (1 folding)

Miracil D or Nilodin is a new remedy recommended for the treatment of schistosomiasis [this *Bulletin*, 1948, v 45, 526]. In this study, 400 mgm were given as a single oral dose to each of 22 male Egyptian patients. The blood concentration was measured by the method of LATNER, COXON and KING [this *Bulletin*, 1948, v 45, 96] with slight adaptations. In patients with normal kidney function, the blood level rose to a maximum at 12 hours and fell almost to zero by 24 hours. The maximum ranged from 60 mgm to 400 mgm per 100 ml. In patients with a renal clearance of less than 50 per cent, the 12-hour blood concentration ranged from 140 to 350 mgm per 100 ml, and the concentration was often still high at 24 hours. Impaired kidney function causes the blood level to be higher and more sustained than it is in normal persons. In order to maintain a persistent high level in the blood, it is recommended that miracil should be given at intervals of 12 hours, with patients who have poor kidney function it may be enough to give it every 24 hours.

F Hawking

GELFAND, M. Cysticercosis of the Brain in the African of Rhodesia. *East African Med J* 1948, Mar, v 25, No 3, 110-12

Between 1940 and 1945, the author found seven cases of cerebral cysticercosis in 2,148 autopsies in Salisbury Native Hospital, Southern Rhodesia. There were also three cases of cysticercosis of the heart, one of which also showed the cerebral form. The cysts were commonly seen in varying numbers over the frontal and parietal lobes and occasionally in the occipital region. In two cases, they occurred on the cerebellar surface. The cysts were always found on the brain surface, but never in its substance.

The Mashonaland African eats locally bred pig, but infected pork is liable to be eaten by him through ignorance, since the same system of meat inspection which exists in more advanced communities is not available to the local African who is therefore more liable to cysticercosis infection than is the European. The author has not seen a case in a white resident of Rhodesia.

The principal clinical feature of cerebral cysticercosis is recurrent epilepsy, with a varying number of seizures. The disease may often terminate in *status epilepticus*. Other mental conditions are described, but the author has not noted them in Africans.

Diagnosis is not easy, and depends on the demonstration of cysts which may not always be detectable by X-ray as calcification does not necessarily occur. Careful palpation may reveal the presence of cysts in the muscles, especially in the arms, shoulder regions and chest wall. They are about the size of a pea, oval or elongated and vary greatly in number.

In the brain, the cysts vary in size from a few millimetres to  $\frac{1}{2}$  in to  $\frac{3}{4}$  in. There may be only one cyst or very many and this variability in size, number and distribution is very great. When the cyst dies, toxic substances are formed which cause necrosis in the surrounding tissues. Later the necrotic tissue becomes fibrosed into a capsule having an inner layer of connective tissue and an outer cellular layer.

PATEL, J. C. Anthelmiasis and Filariasis (*N. bancrofti*) Progress since World War II. *India J. M. & Sci.* 1948, Mar v 2, No. 3, 151-62. [23 refs.]

A general review

D JON L. Kystes suppurrés et abcès chroniques par vers de Guinée. [Suppurative Cysts and Chronic Abscesses caused by Guinea Worms.] *Bull. M/d. de l'Afrique Occidentale F. s. s. s.* 1947 v 4 No. 1, 121-3.

PUBLIC HEALTH REP. Wash. 1948, Apr 9 v 63, No. 13, 478-88. [15 refs.]  
Control of Trichinosis. Report by the Committee on Public Health Relations, the New York Academy of Medicine.

See *Bullet. of Hygiene* 1948, 23 302.

## DEFICIENCY DISEASES

WATERLOW J. C. Fatty Liver Disease in Infants in the British West Indies. *M. Social Research Council. Special Report Series No. 763* 84 pp., 5 text figs. & 26 figs. on 12 pls. [14 refs.] 1948. London H.M. Stationery Office [L.]

Among infants in the British West Indies a syndrome has been observed of which the main features are oedema, muscular wasting and fatty infiltration of the liver. The condition is clearly related to the disease reported from several parts of Africa and known as kwashiorkor or infantile pellagra, but differs from it in that such manifestations of vitamin B complex deficiency as buccal ulceration, fissuring of mucocutaneous junctions and depigmentation of skin and hair which are regarded as characteristic of kwashiorkor are often absent and never severe in the West Indian cases. Fatty change in the liver is regarded as the fundamental lesion and appears in West Indian babies in a relatively pure form, whereas in Africa it appears as part of a multiple deficiency state in which the clinical picture is complicated by the presence of various avitaminoses.

In accordance with this new evidence of liver damage was used as the criterion for selecting the 15 cases described in this report.

In the majority of cases the condition appeared soon after weaning at which time the diet consisted mainly of carbohydrate and contained very little milk. That inadequacy of diet at this period of life is widespread in the West Indies is also shown by weight curves the growth rate falls off markedly during the six months after weaning.

The presenting complaints were oedema and vomiting. There was gross muscular wasting, but subcutaneous fat was not completely lost. In consequence of this and of the presence of oedema the degree of weight loss was less than in many cases of simple starvation. The liver was enlarged, and hepatic failure appeared to be the primary cause of death in four of the six fatal cases.

Further investigation revealed a moderate to severe anaemia which was hypochromic and either normocytic or slightly macrocytic in type. Serum protein concentration was low (less than 4.5 gm per 100 ml. in 8 cases) the reduction being mainly in the albumin fraction. The serum phosphate values were similar to those found in control cases of simple undernutrition; there was slight hyperbilirubinaemia. The only test of liver function which proved of value was the bromsulphthalein clearance test and this showed impairment in all cases. The fat content of the stools was increased; the proportion of pig fat was normal.



Post-mortem examination in four fatal cases showed gross fatty infiltration of the liver, the fat in the liver was neutral fat, the phospholipid content was low. The only other abnormal findings were atrophy of voluntary muscle fibres, atrophy of the acinar cells in the pancreas and a moderate and variable amount of iron pigmentation in the liver.

Fatty infiltration was also demonstrated in surviving cases by means of liver biopsy, and repetitions of this procedure, with serial measurements of serum protein and bromsulphthalein clearance, were used to assess the response to treatment.

Administration of methionine, choline and inositol, in the doses used, appeared to be without effect, on the other hand, improvement occurred on a high intake of milk.

In addition to the 15 cases upon whom detailed investigations were carried out, 600 unselected babies of between six months and two years were examined clinically, and enlargement of the liver without oedema was found in over 10 per cent of them. In two of these cases of symptomless hepatic enlargement, further investigation showed normal serum protein concentration and normal, or almost normal, bromsulphthalein clearance, but liver biopsy revealed the presence of fat. It is concluded that such cases of simple hepatic enlargement represent an early stage of fatty liver disease, and this figure gives some idea of the probable prevalence of this condition.

Cirrhosis of the liver is not uncommon in children in that part of the West Indies where fatty liver disease is commonest. Material obtained by biopsy and at post-mortem upon cases of fatty liver disease provides some evidence that cirrhosis develops as a result of preceding fatty infiltration, and represents the final stage of the disease in those affected who neither die nor recover completely.

As regards the aetiology of the condition, the dietary histories, the absence of evidence of any infection or intoxication and the exogenous source of the liver fat led to the conclusion that fatty liver disease is due to malnutrition. The rarity and inconstancy of associated manifestations of vitamin deficiency suggest that the condition is not due to a specific avitaminosis, and therapeutic tests have shown that it is not due to deficiency of such factors as choline and methionine, which are lipotropic because they act as sources of labile methyl groups. It is, however, clearly associated with a low protein intake and a relative overloading with carbohydrate. Yet the picture is entirely different from that of simple starvation in which the protein intake is often equally low, in that in the latter condition there is loss of all body fat and no fatty infiltration of the liver. The factor determining which of the two clinical and pathological conditions is produced in protein deficiency and protein depletion appears to be the level of caloric intake, deposition of exogenous fat in the liver only occurring when there is a *relatively* high caloric intake.

Waterlow's work is of importance beyond the mere collection of new clinical, biochemical and pathological data about an interesting deficiency state. Although the exact cause of fatty liver disease in infants remains unknown, all that this investigation contributes tends to suggest that the ultimate solution of the problem will be found in an imbalance of nutrient intake, a distortion of metabolic pattern, rather than in any single specific deficiency. Advance has been made in defining the unsolved problems and in showing which of the results of experiments upon nutritional liver damage in animals, here discussed in detail, are or are not applicable to human pathology.

[The finding by Waterlow of a pancreatic lesion is of particular interest. Similar lesions have recently been described by other authors (see below) and the theory has been put forward that pancreatic damage is the fundamental lesion in the syndrome.]

There can be no doubt that fatty liver disease is widespread in the tropics and is an important contributor to the appallingly high infant mortality rate of many tropical territories. Indeed, recent work suggests that the condition is not confined to the tropics (RICHLEY *Lancet* 1948, Mar 27 497). There is here abundant evidence that a high carbohydrate, low protein diet given after weaning is an important, if not the only causative factor. The feeding of pap made from a variety of cereals, with an inadequate intake of milk or other good source of protein, is an exceedingly widespread practice throughout the world and a clear indication is given of the effect that correction of this dietary fault might be expected to have on infant health. Further evidence is produced that the development of cirrhosis of the liver in young people also a common and fatal disease in the tropics, may, in some cases, be traced to fatty liver disease in infancy [See also this *Bulletin* 1947 v 44 841 1948 v 45 635]

Dr I. Smith

HOLMES, E. G. & TROWELL, H. C. Formation of Hepatic Glycogen in Normal Africans and in those suffering from Malignant Malnutrition. *Lancet* 1948, Mar 13, 395-8 2 figs.

The formation of hepatic glycogen was studied in human subjects by estimations on samples of liver obtained by biopsy. As the authors point out, although it has been shown in experiments on animals that liver glycogen increases after glucose is given, this has never yet been directly demonstrated in man. For this reason alone the results are of great interest.

The subjects fasted overnight. In the morning, an initial sample of blood was taken for blood-sugar and serum-protein estimations and the initial biopsy was made. 50 gm. of glucose were then given intravenously and blood samples were taken after one hour and two hours. Biopsies of the liver were made in earlier tests after two hours, in later tests at both one and two hours after glucose had been given. The tests were made on four control subjects, eight patients with malignant malnutrition, one recovered patient, and one with sub-acute hepatic necrosis. With one exception—a child of two years—all the patients with malignant malnutrition were adults. The clinical picture in these cases has already been described (this *Bulletin* 1948, v 43, 363).

In both controls and malnourished subjects, the initial levels of liver glycogen showed wide variation (from about 10 to about 40 mgm. per gm.). In all the controls, the glycogen increased after glucose was given: the increase was sometimes greater at one hour than at two hours. In the patients with malignant malnutrition, the liver glycogen either fell or remained unchanged. In the one case of subacute hepatic necrosis, the initial level was low but was more than doubled two hours after glucose was taken.

The blood sugar in the controls had fallen almost to the initial level two hours after the test dose of glucose. In the malnourished subjects, on the other hand, it remained high. There was therefore a diminished glucose tolerance. Oral glucose tolerance tests in cases of malignant malnutrition showed a similar delayed fall in blood sugar.

The conclusion is drawn that in the patients with malnutrition the liver was unable to synthesize glycogen from glucose at the normal rate. It must, however, have retained some power of forming glycogen from other sources, if not from glucose since it was by no means glycogen-free. Moreover the power to mobilize glycogen could not have been entirely lost, since with one exception hypoglycaemia was not found even after 24 hours fasting. (It is of interest to compare these findings with those of BOSS see *Bulletin* 11 June 1947 v 22, 406) who found impaired glucose tolerance and low resting blood-sugar values in both acute and chronic starvation. See also DAVIES, this *Bulletin* 1948, v 45 633.

J. C. Watkinson

GILLMAN, J., GILBERT, Christine & GILLMAN, T The Bantu Salivary Glands in Chronic Malnutrition with a brief consideration of the Parenchyma-Interstitial Tissue Relationship *South African J Med Sci* 1947, Sept, v 12, No 3, 99-109, 8 figs on 2 pls [27 refs]

The Gillmans and their colleagues in Johannesburg, in their work over a number of years on the pathological histology of malnutrition in Africans, have not confined themselves to descriptive observations, although the facts so gained are of the first importance. They have in addition persistently tried to visualize the reactions of the body as a whole in a particular setting over a period of time—an approach that is both fruitful and stimulating.

The present paper is an example of this. The salivary glands have been little studied by morbid anatomists, because they are regarded as unimportant appendages. In fact, however, they can give useful information, for, as the authors point out, "the modifications in the structure of the salivary glands in human malnutrition represent only a facet of the more general alterations in metabolism, in which many other organs and tissues are implicated."

It is impossible to summarize briefly the details of the histological findings, for these, the original paper must be consulted. The main changes found in cases of malnutrition were —

i Atrophy of the glandular tissue. The acini were reduced in size, or had disappeared completely. Sometimes the cells reverted to a cubical shape, indistinguishable from that of the epithelium lining the small ducts. The serous cells were more susceptible to atrophic changes than the mucous cells.

ii Cystic dilatation of the ducts

iii Patchy accumulation of lymphocytes, particularly near the excretory ducts

iv Low-grade fibrosis, mainly round the ducts

v Cytosiderosis, seldom as severe as in the liver

When atrophy of acini, dilatation of ducts, and fibrosis occurred together, the end-result closely resembled the picture of cystic fibrosis in the pancreas.

In the parotid the changes were rather different. Enlargement of the parotid has frequently been noted in malnourished Africans. This seems to be caused mainly by an increase in size of the individual gland cells, there may also be an interstitial accumulation of fat. Parotid changes of this kind were found almost exclusively in males. Mixed parotid tumour is commoner in Africans than in Europeans, but other neoplasms of the gland are rare.

In the submaxillary and sublingual glands, the range of reactivity was similar to that of the liver, since it included atrophy, fibrosis, and cytosiderosis. Fatty change, however, was less common than in the liver, and less severe. The fact that fibrosis could occur without being preceded or accompanied by fat supports the view previously expressed by GILLMAN and GILLMAN [this *Bulletin*, 1948, v 45, 632] that there is no causal relation between fibrosis and fatty change. Similarly, atrophy and fibrosis occurred quite independently. It is therefore suggested that "an overgrowth of connective tissue, whether it occurs in the liver, pancreas, or salivary glands, does not pre-suppose any observable injury to the parenchyma although such injury may indeed be manifest at the chemical level. However, as in the liver, so in the salivary glands, one form of connective tissue overgrowth seems to be related to factors controlling the distribution of lymphocytes, since fibrosis is commonly associated with lymphocytic infiltration. It is suggested that there may be a general stimulation of the reticulo-endothelial system in response to large molecules, which are either produced endogenously, or absorbed from the gut as a result of defective pancreatic secretion. [For comment, see below] J C Waterlow

MAGALHÃES CARVALHO SCHMIDT M. M. & PÉDRO A. G. Síndrome cecia distrofia plúmcarenal hidropigénica. [Coeliac Syndrome following Nutritional Deficiency with Oedema.] *J. Pediatr.* Rio de Janeiro 1 July 1948 No 7 141-51 3 figs. & 2 graphs. [22 refs.]

In previous papers [this *Bulletin* 1948 v 45 635] Dr Magalhães Carvalho and his colleagues in Rio de Janeiro have described infants and children with oedema, fatty liver and signs of multiple nutritional deficiency. The condition is considered to be identical with kwashiorkor in Africa. They have observed that many cases convalescing from this disease develop, after a few weeks, the clinical picture of the coeliac syndrome. The abdomen becomes protuberant and the stools pale, bulky and offensive. In spite of a voracious appetite the child remains thin and may show residual signs of avitaminosis.

Twenty-four hour specimens of faeces were collected from three such children on a mixed diet, which provided about 24 gm. of fat a day. Three other cases were put for three days on a diet of bananas and butter which was calculated to provide 50 gm. of fat daily. Faeces were collected on the third day. Analysis showed that in both groups the faecal fat content was within normal limits, and the proportion of unsplitted fat was normal, except in one case. The faeces in these experiments were not collected quantitatively, however in other similar cases the total weight of faeces excreted each day was measured and found to be many times greater than normal. It is therefore argued that steatorrhea did in fact exist although it is not apparent from the figures for faecal fat content. The fact that there was no increase in unsplitted fat is attributed to the fat-splitting action of bacteria in the period between collection and drying of the faeces.

The functional capacity of the pancreas was investigated in six cases by measuring the enzyme content of juice aspirated from the duodenum. The child was given no food overnight and a tube was passed into the duodenum. 10 ml. of 33 per cent magnesium sulphate were given through the tube to stimulate bile flow and a sample of bile was collected. Two ml. of warm milk were then given. 20-40 minutes later a sample of juice was aspirated and after a further period of 20-40 minutes a second sample. The trypsin and lipase contents of the samples were measured. Estimations of amylase were abandoned as unreliable. The measurements were made by standard methods and are not described in detail. In all the cases both the trypsin and the lipase content of the duodenal juice were below the lower limit of normal. For trypsin this limit is given as 10 units while the range in the cases investigated was from 2 to 8 units. For lipase the range was from 2 to 30 units, compared with a normal lower limit of 50 units. No measurements were made on control cases.

In discussing their findings, the authors suggest that there may be a connexion between pancreatic damage and fatty liver. They leave open the question of whether there is a definite causal relationship between functional impairment of the pancreas and the clinical manifestation of the coeliac syndrome.

[Although it is necessary, a CILICA staff point out, to avoid the narrow perspectives often resulting from too great a concentration on one gland, such as the liver, yet it is inevitable that in the study of any disease attention should be directed now to one aspect now to another. In the case of kwashiorkor or the focal point of interest at the moment, the pancreas, see this *Bulletin* 1948 v 45 635. In discussing their observations on the exocrine glands the Johannesburg workers have emphasized their causal significance. Examples of the reactions of glandular tissue to malnutrition and as clues to the nature of the relationship between parenchyma and interstitial tissue. But they also have an obvious focal significance because of the close morphological and functional similarity between salivary gland and pancreas.]

The findings of Magalhães Carvalho and his colleagues support the thesis that pancreatic damage is an important feature of kwashiorkor. The interpretation of the Brazilian results taken by themselves, would be difficult, since they were obtained during convalescence, and control subjects were not studied. However, they are in agreement with the work of VÉGHÉLYI in Budapest, who found decreased secretion of pancreatic enzymes in babies not getting milk. This preceded the development of oedema and enlargement of the liver. These observations have not yet been published in detail.

There has been little experimental work on the reaction of the pancreas to dietary deficiencies. FRIEDMANN and FRIEDMANN produced atrophic changes in the acinar cells of the pancreas, together with fatty liver, in rats given a low protein, high fat diet. KRISTAL (*S African J Med Sci*, 1947, v 12, 47) studied the pancreatic changes in rats fed on maize-meal porridge and fermented milk. These rats developed numerous lesions of the liver [see GILLMAN *et al*, *Bulletin of Hygiene*, 1945, v 20, 627]. Histological changes were found in the pancreas in 18 out of 30 rats. These changes included loss of granules, atrophy of acinar cells, cystic dilatation of ducts, fatty infiltration, and occasionally fibrosis.]

J C Waterlow

CHAUDHURI, R N & CHAKRAVARTI, H. An Outbreak of Pellagra Syndrome in a Rural Area of Bengal. *Indian Med Gaz* 1947, Nov, v 82, No 11, 657-60.

An outbreak of disease attributable to multiple deficiency of B-complex factors, in which a pellagroid dermatosis predominated, occurred in one section only of an Indian village. Exact dietary data are not reported, but it is evident that the diet of the whole village was deficient in protein and B vitamins. The only detectable difference between the diet of the affected families and that of those who showed no clinical manifestations was that the rice (which is the staple) of the affected group had many grains which were black in colour and bitter to the taste, whereas that of the affected families had none. The black rice all came from one small area, where the affected families had their paddy fields and where there was scarcity of water.

It was at first considered that the "black" degenerate grains might have lost most of their content of B vitamins, but their nicotinic acid content proved, upon analysis, to be within normal limits. It is possible that these "black" grains contained a toxic substance which precipitated the occurrence of the deficiency state.

Dean A Smith

BORKOW, A, FOWDEN, L, STEDMAN, M M, WATERLOW, J C & WEBB, R A. A Growth-retarding Factor in Maize Bran. *Lancet* 1948, May 15, 752-3, 1 fig.

An outstanding feature of endemic pellagra is its frequent association with the consumption of maize as a staple cereal. ALKROYD and SWAMINATHAN showed [this *Bulletin*, 1940, v 37, 797, *Bull Office Internat d Hyg Publique* 1941, v 33, 507] that this cannot be explained on the basis of nicotinic acid deficiency alone. In the search for a toxic or pellagragenic factor in maize it has been shown that this cereal if fed in sufficient quantities, exercises a growth-retarding influence in rats (WOOLLEY *J Biol Chem*, 1946, v 163, 773, KREHL, HENDERSON, DE LA MUERGA and ELVENJEM, *ibid*, v 166, 531), the latter workers attributing the effect to amino-acid imbalance, especially in respect of tryptophan.

In 1947 two of the present authors investigated an apparent increase in pellagra in Basutoland and found evidence that this increase was related to an increase in the consumption of maize bran resulting from changes in milling practice.

Feeding tests have now been made upon weanling mice by means of firstly a diet containing 10 per cent. bran, secondly a diet comprising mostly bran-free maize flour and a standard diet. The diets contained 10 per cent. protein and were designed to avoid, as far as possible any amino-acid imbalance tryptophane being available in equal amounts in the test and control diets.

The animals fed upon the 10 per cent. bran diet showed a highly significant growth retardation when compared with control litter mates. No such growth-retardation occurred in the animals fed upon the maize flour diet nor in a series fed upon the 10 per cent. bran diet to which 5 mgm. nicotinamide per 100 gm. had been added.

This evidence most strongly suggests that the toxic factor in maize whose effect for rats and mice is growth retarding resides in the bran fraction and that the bran-effect is preventable by nicotinic acid. Extraction of the toxin has not yet been achieved.

As the authors emphasize retardation of growth in mice has no necessary reference to human pellagra. It is, however of the greatest importance to determine whether the factor in maize bran which has been shown to be growth-retarding for mice is toxic to man and whether it has any relation to pellagra. The results of work on these lines, which is now going on, may prove an important step in elucidating the aetiology of endemic pellagra.

Dean I. Smith

FRANKLAND A. W. Deficiency Scrotal Dermatitis in P.O.W.s in the Far East.  
*B. M. J.* 1948, May 29 1023-R. (19 refs.)

Scrotal dermatitis associated with dietary deficiency was extremely prevalent among allied prisoners of war in the Far East. The present description is based upon 351 cases observed on Singapore Island.

Four forms, or degrees of the condition were recognizable clinically: (i) Mild acute dry in which there was redness and irritation of the scrotum under treatment or sometimes spontaneously a fine desquamation left apparently normal skin. (ii) Severe chronic dry bright red erythema extending to thighs, penis, perineum and anal region. (iii) Chronic wet weeping dermatitis of scrotum and thighs which without treatment then developed into (iv) ulcerated and oedematous with great swelling heavy secondary infection sometimes with *C. d. phloeris* progressing in the worst cases to prethrombosis, gangrene which with marked generalized toxic symptoms, sometimes terminated fatally.

The incidence of the condition was highest when the riboflavin content of the diet was low conversely when the latter could be kept at an adequate level cases did not occur. Associated deficiency diseases both in individuals and in general incidence were those usually attributed to hyporiboflavinosis namely glossitis, cheilosis, angular stomatitis and corneal degeneration.

Some success was achieved by various forms of local treatment but this was often incomplete and the relapse rate high. On the other hand, Marmal appeared to have a specific curative effect in uncomplicated cases and greatly hastened recovery in those cases for whose secondary infection local treatment was necessary.

The aetiology of the condition is discussed and it is concluded, on a considerable weight of evidence that this form of scrotal dermatitis is due to deficiency of riboflavin or of some factor closely allied to it. Dr. I. Smith

CHEN TZU-TA Angular Blepharitis in Ariboflavinosis—a not well known Clinical Manifestation of Riboflavin Deficiency *Chinese Med J* 1948, Jan, v 66, No 1, 1-4

"Three cases of angular blepharitis occurring as a manifestation of ariboflavinosis are described. A survey in a prison in Nanking was made. Twenty-three out of the 97 prisoners examined were found to have ariboflavinosis and 4 out of these 23 had angular blepharitis. This sign has not yet received much attention as a clinical manifestation of ariboflavinosis."

## DERMATOLOGY AND FUNGUS DISEASES

SALVIN, S B Complement Fixation Studies in Experimental Histoplasmosis *Proc Soc Exper Biol & Med* 1947, Nov, v 66, No 2, 342-5, 2 figs [11 refs]

In some recent work on the complement-fixation test for the diagnosis of histoplasmosis, by TENENBERG, HOWELL, FURCOLOW & BUNNELL [this *Bulletin*, 1948, v 45, 644], and by CROSS & HOWELL [this *Bulletin*, 1948, v 45, 643] the antigens used were histoplasmin (a filtered autolysate of the mycelial growth of *Histoplasma capsulatum*) and the polysaccharide extracted from histoplasmin. SALVIN, on the other hand, used, as antigen, the intact, formalin-fixed, yeast-like form of the fungus, designated "YP", which was cultivated on a special medium devised by him [*Bulletin of Hygiene*, 1948, v 23, 360].

Rabbits inoculated intravenously with living cultures of *Histoplasma capsulatum* in the yeast form, yielded an antiserum which reached its highest titre (about 1:512) in 30 days. Six different strains of *H. capsulatum* were used and the sera of 15 immunized animals were tested for complement-fixation with the YP and crude histoplasmin antigens. All of the sera reacted strongly with the YP antigen, the highest titre being 1:512, but only 8 reacted with the histoplasmin antigen, the highest titre not exceeding 1:128.

On the matter of the specificity of the complement-fixation test for histoplasmosis, the YP antigen gave no reaction whatever with 10 human sera from cases of coccidioidomycosis, 8 anti-*Coccidioides* rabbit sera, 8 anti-*Blastomyces* rabbit sera and 4 anti-*Candida* rabbit sera, but the histoplasmin antigen gave a reaction, albeit in low titre, with some of the sera in each of these groups. The specificity of the complement-fixation reaction with the YP antigen was also demonstrated in a test with 30 human sera from healthy persons and 2 sera from cases of histoplasmosis.

J T Duncan

## HEAT STROKE AND ALLIED CONDITIONS

NELSON, N, EICHNA, L W, HORVATH, S M, SHELLEY, W B & HATCH, T F Thermal Exchanges of Man at High Temperatures *Amer J Physiol* 1947, Dec 1, v 151, No 2, 626-52, 15 figs

In the study of physiological responses to high environmental temperatures, there is a great need for relationships to be established whereby the thermal stress imposed by the environment can be described in terms of the various factors which together make up that environment. The present paper describes a calorimetric study of the thermal exchanges between man and his environment. The total heat exchange was broken down into its several components, and physical constants were determined. The observations were made on

healthy young men exposed to dry bulb temperatures ranging from 80 to 120°F with wet bulb temperatures of 70 to 91 and wind speeds of 30 to 600 feet per minute. Experiments were done with the subjects standing nude or clothed, and walking while clothed. The walking tests were done on a treadmill at a speed of three miles per hour with a three per cent. gradient. The metabolic rates while walking were about 160 Cal. per sq. m. per hour. The temperature and humidity of the air, the speed of air movement, and the radiation from the walls were measured during each test period. Measurements on the subjects included rectal temperatures, skin temperatures at various points, surface temperatures of clothing, oxygen consumption, heart rate, evaporated sweat loss and total sweat loss. From the temperatures of the skin and of the surface of clothing, weighted mean skin and surface temperatures were calculated.

In nude subjects, the maximum coefficient of evaporation varied as the 0.4 power of the air velocity. It is remarked that in evaluating the influence of wind speed and vapour pressure on the rate of evaporation the study must be confined to conditions where the skin or clothing surface is completely wet. With low rates of sweating the rate of evaporation is not influenced by wind speed. Sweating rates high enough to measure the maximum coefficients of surface evaporation in clothed men were probably not reached, but charts are given which show the coefficients actually found.

The coefficients of convection vary as the square root of the air velocity. The convection coefficients for clothed subjects were 23 to 41 per cent. higher than those for nude subjects. This is in agreement with the estimated differences between the surface areas of clothed and nude men.

The radiation coefficients of nude subjects agreed with the theoretical value based on emissivities of wall and skin of 1 and a radiation area of 91 per cent. of the geometric area of the body. For some unaccountable reason the coefficients of radiation for clothed subjects were much lower than would be predicted from reasonable assumptions as to the surface area and emissivity of the clothing.

Movement of the arms and legs while walking resulted in an increase in the apparent wind speed. When the men were walking at three miles per hour this apparent increase was 150 feet per minute above the wind speed in the tunnel.

T. Bedford

NELSON, A. A., SHELLEY, W. B., HOSFATH, S. M., EICHMA, L. W. & HATCH, T. F. The Influence of Clothing, Work, and Air Movement on the Thermal Exchanges of Acclimatized Men in various Hot Environments. *J. Clin. Investigation*. 1943, Mar. 27, 22, 209-16, 4 figs.

Partitional-calorimetric studies were made of four well-acclimatized young male subjects. They were acclimatized by walking for four hours a day while dressed in trail uniforms, in an environment with a dry bulb temperature of 120°F and a wet bulb of 86°F. The calorimetric tests were carried out in a wind tunnel placed inside the laboratory hot room. The men stood or walked on a treadmill. The walking was at a speed of 3 miles per hour with a grade of three per cent. Walking caused an average energy expenditure of 160 Cal. per sq. m. per hour and standing caused one of 135 Cal. per sq. m. per hour. Seven temperature levels were studied. In these the dry bulb temperature ranged from 80 to 120°F and the wet bulb from 70 to 91°F. At each temperature level wind velocities of 30, 50, 150, 300 and 600 ft. per minute were employed. At each condition three men were studied standing nude, standing clothed and walking clothed. The men spent 7½ hours in the heat each day except Sunday.

Increasing the wind speed from 30 to 600 feet per minute did not cause a striking change in the rectal temperature—in no case was the average rectal



temperature changed  $1^{\circ}\text{F}$ . Such an increase in air movement generally caused significant reductions in the skin temperatures of the subjects. The surface temperatures of clothed men followed the same pattern as skin temperature until the air temperature exceeded  $96^{\circ}\text{F}$ . With air temperatures higher than body temperature, the surface temperature of the clothed body rose with increasing air movement and occasionally reached  $105^{\circ}\text{F}$ . When the air temperature was  $120^{\circ}$ , the total sweat loss of clothed subjects was strikingly reduced by increase in air movement. With wet bulb temperatures of  $88^{\circ}$  or  $91^{\circ}\text{F}$ , increase in air velocity caused appreciable reductions in pulse rates.

The body heat production for a given amount of work remained unchanged irrespective of change in environmental conditions. When at high temperatures resting men wore clothing they gained less heat by convection and radiation than when they were nude, and therefore their evaporative heat losses were smaller.

T Bedford

ADOLPH, E. F. **Tolerance to Heat and Dehydration in Several Species of Mammals** *Amer J Physiol* 1947, Dec 1, v 151, No 2, 564-75, 11 figs [27 refs]

Comparisons of tolerance to heat and dehydration were made between several species of mammals. The species considered were dogs, cats, rabbits, guinea pigs, rats, and mice. These vary greatly in their capacities of evaporation, cooling, and in the tissue temperatures that they can endure. Together with body size, these appear to be the principal factors which determine tolerance to heat. A consistent sign of lethal conditions was found to be a rectal temperature of between  $41.7^{\circ}$  and  $43.4^{\circ}\text{C}$ , the critical value varying with the species. It appeared that heat stroke resulted from hyperthermic injury to regulatory tissues which were not identified. In some instances when animals had been subjected to gradual increase of rectal temperature and then cooled, death was delayed for periods up to 26 hours.

Dehydration through panting was copious in cats and dogs, but was limited in the other species. A considerable degree of dehydration did not bring about any change in the rate of evaporation loss. Dehydration rendered the animal very sensitive to warm atmospheres, presumably owing to the limitation of the circulation brought about by a depleted plasma volume. Failure of the circulation to transport heat to the surface caused an explosive rise of rectal temperature. In hot atmospheres animals that were allowed water to drink at will did not drink enough to maintain their body weights, and, except in the case of dogs with only small water deficits, when deprived of water they subsequently drank less than enough to recover their body weights.

T Bedford

GROCOTT, J. F. L. **Comfort Cooling in the Tropics** *J Inst Heating & Ventilating Engineers* 1948, Apr, v 16, No 153, 36-64, 9 figs [28 refs] Discussion 64-79

In planning an installation for cooling buildings in the tropics one should be able to ascertain the following meteorological data —

- (a) maximum temperature for each month and season,
- (b) average maximum for each month,
- (c) average summer maximum,
- (d) the number of days on which the average summer maximum is exceeded in steps of  $3^{\circ}\text{F}$ , e.g., if average maximum is  $110^{\circ}\text{F}$  how often is  $112^{\circ}$  exceeded and how often  $115^{\circ}$  and so on.

Design recommendations are made on the basis of the experience of the Anglo-Iranian Oil Company during the past 20 years. When the external

healthy young men exposed to dry bulb temperatures ranging from 80° to 120° F with wet bulb temperatures of 70° to 91° and wind speeds of 30 to 600 feet per minute. Experiments were done with the subjects standing nude or clothed, and walking while clothed. The walking tests were done on a treadmill at a speed of three miles per hour with a three per cent gradient. The metabolic rates while walking were about 160 Cal. per sq. m. per hour. The temperature and humidity of the air, the speed of air movement, and the radiation from the walls were measured during each test period. Measurements on the subjects included rectal temperatures, skin temperatures at various points, surface temperatures of clothing, oxygen consumption, heart rate, evaporated sweat loss and total sweat loss. From the temperatures of the skin and of the surface of clothing, weighted mean skin and surface temperatures were calculated.

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Design recommendations are made on the basis of the experience of the Anglo-Iranian Oil Company during the past 20 years. When the external

temperature ranges from 90°F to 125°F the internal temperature should be 75 to 83. This range has been used as the basis for all buildings except the general hospital. In the hospital, a uniform condition of 75°F with 50 per cent. relative humidity is required in summer while in winter the requirement is 70°F with 30 to 50 per cent. relative humidity. In operating theatres a temperature of 70°F with 50 per cent. relative humidity is demanded all the year round although the external temperature ranges from 40°F to 120°F. The changes between external and internal conditions are sometimes very great. Experience has revealed no ill effects of these contrasts, while great benefits have accrued to the patients.

There are notes on the relation of building construction to air cooling. Modern buildings are constructed on the conventional lines of similar buildings in temperate zones. The roofs are mostly flat or of slight pitch, and constructed of tile on insulation. Full advantage is taken of verandas, canopies, Venetian slats, etc. to exclude sunlight and most buildings are finished in light colour. There is also a detailed discussion of the appropriate methods of cooling various types of buildings.

T. Belford

### MISCELLANEOUS DISEASES

F. DE L. Contribution à la pathologie du Congo. [Notes on Pathological Conditions among the People of the Congo.] *J. n. Soc. Belge de Méd. Trop.* 1947 Dec. 31 v. 27 No. 4 433-40.

LIEBOW, P. Quelques notes à sujet de la pathologie indigène dans l'Éthiopie. [Notes on Pathological Conditions in Ethiopia.] *J. n. Soc. Belge de Méd. Trop.* 1947 Dec. 31 v. 27 No. 4 441-6.

DARMALL, G. Une schématisation sur la pathologie des indigènes à Kwango. Observations de 1938 à 1945. [Descriptive Note on Pathological Conditions among the Africans in Kwango between 1938 and 1945.] *J. n. Soc. Belge de Méd. Trop.* 1947 Dec. 31 v. 27 No. 4 429-32.

BERTOLO A. & LARGO G. Contributo isto-patologico allo studio della gangrena (rimo-oro-faringite mortale dei tropici). [Histological Study of a Case of Gangrene; *Acta Med. Italica*. 1948 I b v. 3, No. 2, 32-8, 10 figs. (13 refs. English summary)]

The authors relate the case of an Arab woman 52 years of age who had first shown signs about 20 years ago of a small painless nodule affecting the left nostril, rapidly breaking down and spreading till much of the nose, mouth and face was destroyed by a typical gangrene. A series of photographs depicts graphically the terrible state of this unfortunate woman. Search for *Mycobacterium* and for *Mycobacterium tuberculosis* was repeatedly negative also for *Trophozoites*, *Leishmania*, rhinoscleroma and blastomycetes. The W.R. had once been reported positive in 1929 but was negative in each of the next three years. The Kahn and Meinicke tests were always negative. All sorts of treatment were tried—arsenicals, mercury, bismuth, antimonials, sulphonamides, etc. etc. but all in vain and the patient died.

Histological examination of the various tissues and organs was made of different parts of the local lesions of the lung, heart, liver, spleen and kidneys. Photomicrographs indicate the condition found but there is nothing characteristic in them and none of the changes characteristic of leprosy, tuberculosis (including lupus), syphilis, or rhinoscleroma was to be made out and the authors see no reason for regarding gangrene as a complication or sequel of

yaws, they incline to the view that it is distinct from all of these, in short, that it is a condition *sui generis*, or in the medical jargon of to-day a "separate clinical entity"

H Harold Scott

ORTNER, E Ueber Lathyrismus  
May 7, v 60, No 18, 291-3

[On Lathyrism] [11 refs]

The author states that in the concentration camp at Vapniarka, near Odessa, lathyrism was very rife. Of about 1,400 inmates, 800 or 57 per cent showed the disease in an early or late stage. In September 1942, 1,200 men came to the camp they had been in confinement for more than two years in different Rumanian prisons on "political or racial grounds". They were in a poorly nourished state and their food in the camp consisted of only 400 gm of cooked *Lathyrus sativus* and 200 gm of bread made of 80 per cent barley meal and 20 per cent chopped straw. Their chief complaints were of cramps, mostly in the calves, but also in the arm muscles, strangury and frequency of micturition, up to 20 times a day. Within two months walking became increasingly difficult, with spastic paresis. Ulcers would form on the toes, especially the big toe, and progress to gangrene, in many cases symmetrical and ending fatally. Three cases are described in detail.

H Harold Scott

## ENTOMOLOGY AND INSECTICIDES GENERAL

ANDUZE P J Fauna hematófaga del Distrito Maturín (Est Monagas, Venezuela)  
los Culicidos [The Mosquitoes of Maturín District, Monagas, Venezuela]  
Rev Med Vet y Parasit Caracas 1947, Jan-Dec v 6, Nos 1/4, 121-6

STAGE, H H DDT to control Insects affecting Man and Animals in a Tropical Village J Econom Entom 1947, Dec, v 40, No 6, 759-62, 1 fig

During a period of five weeks in March and April 1946, all animals (except three calves) and all surfaces of buildings, inside and out, in Moengo, a village in Surinam, South America were treated with either 2.5 per cent DDT suspension in water or with 5 per cent DDT oil solution.

The author describes the formulations, spraying equipment and the methods of trapping and then notes the effectiveness against certain insects. After two weeks, mosquitoes were difficult to find in cowbarns, but they began to be caught again after ten weeks. The numbers in light traps in the centre of the village fell from 900 and 400 to 13 and 3 respectively, a few days after treatment, 'later there were even fewer. In a house treated with the DDT suspension, mosquitoes were released two to three months after treatment and all were dead in three to four hours after eleven months, 2,000 others were released and 60 per cent were dead after seven hours. In a similar house treated with the DDT oil solution, 2,000 mosquitoes were released after eleven months some were still alive after 24 hours, but 50 hours later only two could be found alive. The species used in these tests are not named, but a complete analysis is to be published elsewhere. A list of species found in the locality is given.

Horn flies, bed-bugs, fowl ticks (*Argas persicus*) and chigoes (*Tunga penetrans*) are thought to have been eradicated. The number of cockroaches (? *Periplaneta americana*) is said to have been reduced by 90 per cent and there was a

reduction in the number of cattle ticks (*Boophilus annulatus macroplus*). The programme for dealing with dog fleas broke down, and dogs are still infested.

H. S. Levine

## LABORATORY PROCEDURES

BLACK, R. H. Leishman's Stain adapted for Use with Histological Sections. *Ann Trop Med. & Parasit.* 1948, Apr. v. 42, No. 1 5-3 3 figs. in 1 pl.

This method is recommended as an alternative to Giemsa's stain for sections, particularly to demonstrate the erythrocytic and exoerythrocytic forms of *Plasmodium gallinaceum*. Thin sections are treated for 5-10 minutes with a saturated aqueous solution of picric acid. They are then washed in water and stained for 25 minutes with a mixture consisting of one part of Leishman's stain with two parts of distilled water. This should be freshly prepared. The section is then immersed in running water for about 10-15 minutes, dehydrated in xylol-acetone mixtures and mounted in a neutral mounting medium. Van Gieson's stain was originally employed, but tests showed that it was the picric acid constituent which was responsible for the good results. This substance appears to act by virtue of its acidity. Its pH was 12, and when decinormal hydrochloric acid was substituted for picric acid essentially similar results were obtained. The tissue cells stain brilliantly and in some organs, differentially. In the kidney, for instance, the collecting tubules are stained magenta, while other tubules give a different reaction. Malaria parasites in red blood cells are easily recognized, and exo-erythrocytic forms are very deeply stained.

The author admits that the method is not an improvement on Giemsa's stain and the absence of differential staining of the chromatin and the cytoplasm of parasites will detract from its value in protozoology. P. C. C. GORDON

## REPORTS, SURVEYS AND MISCELLANEOUS PAPERS

NEDERL. TIJDSCHR. V. GENESK. 1948 May 22, v. 92 (ii) No. 4 1566-80  
2 graphs. Nederlandse vereniging voor tropische geneeskunde.  
Vergadering op zond. 25 September 1947 t. Utrecht (HUTTENLOFF, A. A. President). [Netherlands Association for Tropical Medicine.]

Four subjects were dealt with at this meeting held at Utrecht in September 1947: plague, tetanus, the beriberi heart and malaria.

Two methods of campaign against plague have prevailed in Java: the housing of the indigenous population, with protection against rat intrusion and prophylaxis by means of living plague vaccine. The vaccination languished under Japanese occupation and the occurrence of abscesses after inoculation raised the suspicion that these were mitigated plague lesions. These were however only manifestations of contamination by pyogenic organisms and the plague bacillus in question was proved to be full just a virulent. In the restoration of the vaccine of Otten the Harbin strain has now been left out and only the original Tywidet strain used. The latter strain immunized the guinea-pigs in minimal doses but not the house rat. It is the guinea-pig, which owes death to man in its immunological response and the Tywidet strain is therefore to be preferred for routine use. Protection is reduced for three months unaltered and to a less degree for an entire year.

A close argument on the characteristics of the beriberi electrocardiogram was presented by AALSMEER mainly to show how this differed in oriental regions from that of America and the west. The conclusion seems to be reached that the western beriberi heart is not of the same type as the oriental *shoshun* and that recognition of an alcohol-beriberi heart must be given consideration.

Malaria is treated under the heading of "Colonization Kesir," which signified really the establishment by the Japanese of a concentration camp in a region full of all the possibilities of intense malaria infection. The vector mosquito was *A. aconitus*. Very careful work was done both in the way of records and of quinine prophylaxis. The records, which would have given valuable information on the incidence of relapses and fresh infections, were lost. A most fortunate circumstance in this camp was that quinine was available in abundance which, with the energetic measures adopted to deal with the mosquito menace, served to bring malaria under medical control. This régime followed on the first explosive outbreak of malaria. Orderlies were appointed who made daily visits to their sector of the camp. Slight cases of sickness were reported and examined the same day. If the patient had fever, a thick drop preparation was made of his blood and if it was positive he received a first treatment of 30 tablets of bisulphate of quinine—6 each day, of 220 mgm each. After a week's interval he received the same 5-day course again. A table showing the frequency distribution of attacks in 295 cases is given, where the greatest number, 130, suffered only one attack and the numbers fell steadily to 3 cases with 9 attacks each.

W F Harvey

POPPER, L. *Medizinisches aus Bolivien* [Medical Notes from Bolivia] *Wien Klin Woch* 1948, May 14, v 60, No 19, 297-301

An interesting though short account of the diseases met with in Bolivia prefaced by some facts on the physical geography of the country. There are [or were, at the time of writing] 500 doctors practising there, most of them in the towns. *Tuberculosis* has been recorded as common among the soldiers, and the author's predecessors have stated that 7 per cent of the regiment of 400 die of it. The author, therefore, undertook an investigation, examining all recruits. An intracutaneous test showed 38 per cent reacting positively. Further observation of the members of one unit discovered no cases in the next three months. Later, some, especially those who had not reacted to tuberculin, developed an exudative pleurisy and a few of them actual pulmonary tuberculosis. By careful attention the fatality rate fell from 7 to 1 per cent. Another unit not so controlled and watched over, and housed in unfavourable conditions, had a 10 per cent mortality in six months. Symptoms, in the earlier stages at least, are very slight. In the following year 3,540 men were kept under observation and among them were 65 cases of pulmonary tuberculosis, 58 of exudative pleurisy, and 19 of other forms, 142 in all, or 4.0 per cent morbidity [not 152 and 4.3, as stated]. *Dysentery* also is fairly rife, some amoebic but more commonly bacillary—the water, from ponds and wells, is often contaminated. *Leishmaniasis* is not seen in Chaco, but occurs in north-east Bolivia. Other ulcerous conditions met with are phagedaena (associated with spirochaetes and fusiform bacilli and occasionally diphtheroids) and blastomycosis, but this last is uncommon. The author has seen one case of coccidioidomycosis. *Malaria* is, of course, present, mostly benign tertian the relative frequencies of benign tertian, subtertian and quartan are said to be 30:3:1. Chronic malaria is often afebrile, but the parasite can nearly always be found, it was missed in only 4 per cent of 600 cases. No case of blackwater fever was seen by the author. Nutrition is poor and consequently resistance to disease is low. The average diet for an adult is only 1,600-1,800 calories

and that mainly made up of carbohydrate. In the Bolivian highlands, the amounts consumed per head per year are 21 kgm. meat 36 litres of milk and 0.22 kgm. of fat— the lowest in the world. In the lower levels where cattle are reared, the quantities of meat and milk are greater but the calorie value is lower. The soldier's ration is about 3000 calories but the constituents are badly balanced.

Hookworm infestation is widespread and severe anaemia is far from uncommon both *Ancylostoma* and *Necator* are the cause. About 70 per cent. of recruits were passing hookworm ova, 20 per cent. *Acaris* 15 per cent. *Trichuris* and 6 per cent. *Strongyloides stercoralis* ova. *Balanitium* also is common. *Filaria*s especially *M. oswaldi* is often met with. Chagas disease is not very common in spite of the fact reported by many that *Triatoma infestans* and *Panstrongylus megistus* were seen and the author found more than half of them infected. Leprosy was occasionally seen. Yellow fever has been almost stamped out by the efforts of the Rockefeller Foundation. Eaters of Coca suffer from paresis and neuro-muscular atrophy especially of the peroneal area, and from hyperaesthesia and anaesthesia of the conjunctiva later those who indulge in this habit become wrecks and succumb readily to intercurrent disease. Venereal diseases are not rare lympho-adenoma inguinale is fairly common. Of the infective fevers *d. pluvialis* is rare scarlet fever practically unknown measles occurs inland and among adults whooping-cough in children is usually mild.

H. Harold Scott



# TROPICAL DISEASES BULLETIN

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[No 9

## SUMMARY OF RECENT ABSTRACTS\*

## VII HELMINTHIASIS

[Continued from p 669]

*Nematodes*

*General*—STOLL (p 667) must be read in the original, he has written a valuable study, under the title of *This Wormy World*, of the probable incidence of human helminthiasis

In his account of a helminthological survey of N Rhodesia, BUCKLEY (p 909) points out that as the Africans eat any part of the carcass of animals, the presence of eggs of certain worms in human stools does not prove true infection—the eggs themselves may have been ingested in the meat eaten *Necator americanus* was the only hookworm found in this survey, and the incidence of infection was higher in cassava plantations (usually situated near villages) than in millet plantations (further away and probably with more scattered faecal deposits) *Strongyloides fülleborni* and *S. stercoralis* were also found, but *Ascaris lumbricoides* was not widespread. The last is usually associated with a congested population *Acanthocheilonema perstans* was found in about 6 per cent of blood specimens examined, but *Wuchereria bancrofti*, *Onchocerca volvulus* and *Loa loa* are not endemic

EINHORN and MILLER (p 215) have summed up their series of studies on intestinal helminthiasis in children of the Panama canal zones. They discuss age incidence, symptomatology and treatment

LOUGHLIN and STOLL (p 335) describe an acid-ether-xylol technique for examination of faeces for helminth eggs. Tests indicated that this gave better results than the Telemann and DCF techniques with *S. japonicum*, *Trichuris* and infertile *Ascaris* eggs. The test is described in detail

OLIVER-GONZÁLEZ (p 729) discusses the immunological relationships between polysaccharides derived from various infecting organisms, including several worms parasitic for man, and pneumococci. Cross-reactions, and the techniques used, are discussed in the original paper, which should be consulted

*Hookworm Infestation etc*—CANTACUZÈNE and LUPASCO (p 529) have found hookworm infection in coal miners in Rumania where in some mines the rate of infection reaches 96 per cent. The sanitary conditions in the mines are bad, the atmosphere is warm and damp and the miners usually work barefoot

\*The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin* 1947 v 44. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed

Clinical signs include digestive troubles, nausea, vomiting, epigastric pain and occasionally diarrhoea. KAMALOV *et al* (p. 224) describe a focus of hookworm infection in Georgia, Russia.

STOLL *et al* (p. 441) show that the incidence of hookworm infection is much higher in United States troops from the southern coastal States than from other parts, the majority of the worms being *Necator*. In troops exposed to infection in the Philippines most of the worms were *Ancylostoma*. There was no correlation between egg count and haemoglobin percentage, and very little between high egg count and high eosinophilia. There is good evidence that infection may be acquired by launderers who handle soiled garments which have been allowed to stand for several days in a damp condition. LONGHILL and STOLL (p. 735) take up this point. They have proved that active filariform hookworm larvae may be found in large numbers in blankets and nightclothes of patients with hookworm infection, if these are damped repeatedly and kept for several days. The larvae can migrate several inches. Launderers have been infected in this way in Guam and no doubt similar infection may be spread in hospital patients if the bed-clothes are dirty and damp.

KAMALOV (p. 608) has shown that infective hookworm larvae are capable of climbing vertically on blades of grass to a height of 22 cm, provided that there is a film of moisture on the grass. A person coming into contact with these larvae may be infected, even if wearing shoes and socks.

MOST *et al*. (p. 443) found hookworm infection in 6.7 per cent. of American soldiers who had not been outside the United States, and in 11.5 per cent. of soldiers who had served in the Pacific theatre. At an American Army General Hospital in the South Pacific, hookworm infection was found in 13 per cent. of those examined; other nematodes were also found.

BLACK (p. 336) discusses the co-existence of tuberculosis and hookworm infection in Florida, where the latter is prevalent. The association of hookworm infection and sputum positive for tubercle bacilli, or of hookworm anaemia with tuberculosis, indicates a relatively unsafe verminous prepossession. HERBERTS (p. 225) refers to the relationship between anaemia due to hookworm disease and lack of iron in the diet, and the disease known in West Africa as dibolia, which in some respects resembles kwashiorkor.

CHAUDHURI and MUKHERJI (p. 800) report a case in which tetrachlorethylene appeared to be the immediate cause of death, but the patient was very emaciated as a result of gross malnutrition. It is probably wise to withhold even such safe drugs as tetrachlorethylene from patients in this condition.

WRIGHT and GOLD (p. 224) have found 26 cases of the Loeffler syndrome in 78 patients with creeping eruption thought to be due to *Ancylostoma braziliense*. They think that the pulmonary infiltration is an allergic reaction to antigens from the larvae in the skin. The systematic treatment of creeping eruption due to *Ancylostoma braziliense* with drugs is disappointing. HITCH (p. 91) found no definite evidence that certain antimonials and one arsenical had any lethal effect on the larvae, though they did relieve some of the symptoms, probably through a larvostatic action. ASTARF (p. 836) has observed human infection with *Uncinaria stenocephala*, a hookworm of certain carnivores. Larvae were detected in the many small skin pustules. The mode of infection was not clear, though the author suspected a dog, which commonly slept with the patient.

HARTZ (p. 101) has given a detailed description of the pathological changes found in the intestinal wall in a case of strongyloidiasis with intestinal auto-infection. The post mortem examination was made 40 minutes after death, and the findings cannot therefore be attributed to post mortem change. Details cannot well be abstracted further and should be sought in the original.

GILLMAN (p. 1067) states that in Indo-China the type of *S. stenocephala* commonly found usually shows the indirect (sexual) cycle of development but

that the direct (asexual) cycle also occurs This is the reverse of the position in temperate climates, but the view (expressed by some workers) that the direct cycle does not occur in the tropics is wrong

WATSON (p 337) sums up the points of differentiation between hookworm, *Strongyloides* and *Trichostrongylus* infections

DE OLIVEIRA (p 96) prefers a preparation of carbon tetrachloride and oil of chenopodium for hookworm infection, and gentian violet for *Strongyloides* *Ascaris*, etc — *Ascaris* and *Trichuris* were found in almost all the inhabitants of a Portuguese village (DE MEIRA and CORRO p 1014) Hsu (p 1008) made a survey of intestinal parasites in school children and in university freshmen and servants, in Chengtu, where *A. lumbricoles* was common *Ascaris* is also common in New Orleans, and SWARTZWELDER (p 225) shows that the chief symptom associated with it is abdominal discomfort, fever is quite often present Intestinal obstruction occurred in 18 of 202 cases BARBER (p 736) refers to the surgical aspects of *Ascaris* infection, quoting several cases from Cyrenaica

OLIVER-GONZÁLEZ (p 226) has investigated the functions of the non-immunizing antigens present in *Ascaris lumbricoles* The subject is complicated and is related to blood groups, the paper should be read in the original

MUKERJI and BHADURI (p 836) report quite favourably on certain indigenous drugs, derived from Indian plants, in the treatment of *Ascaris* infections

Filaria — FLOCH (p 103) shows that in a group of people in French Guiana the incidence of *W. bancrofti* was of the order of 12–18 per cent of adults *Culex fatigans* is apparently the sole vector He discusses the relationship between elephantiasis and filariasis, concluding that elephantiasis may arise as a result of chronic streptococcal infection, and doubting its aetiology connexion with filariasis FLOCH and DE LAJUDIE (p 922) found *W. bancrofti* in 12–13 per cent of Creoles in French Guiana

HERNÁNDEZ MORALES and GONZÁLEZ BARRIENTOS (p 228) found microfilariae of *W. bancrofti* in the night blood of 4.35 per cent of 1,256 prisoners in Porto Rico, and BERCOVITZ and SHWACHMAN (p 338) found them in the night blood of 3.42 per cent of young Porto Ricans, very few of whom gave clinical histories consistent with filarial disease

In part of Hyderabad the incidence of filarial disease was found by FAROOQ and QUTUBUDDIN (p 669) to be 0.2 to 4.9 per cent Microfilariae were found in only 1 of 138 persons with filarial disease, but in 15.5 per cent of 584 apparently normal persons Most of the microfilariae were *W. bancrofti* (92.4 per cent) *W. malayi* was found in 7.6 per cent *Culex fatigans* is the only proved vector, but species of *Mansonia* were present in the vicinity

Examination of two American soldiers with filariasis contracted in the South Pacific showed that the microfilariae of *W. bancrofti* were present in the peripheral blood in greater numbers during the day than during the night, though they were never absent EYLES *et al* (p 837) think that these microfilariae showed a degree of diurnal periodicity rather than, as is usually accepted, no periodicity Microfilariae of *W. bancrofti* found in the Central Philippines show modified periodicity (AVERY, p 445)

FOSHAY (p 837) describes the cuticular morphology of certain microfilariae PRATT and NEWTON (p 104) have studied in detail the progress of embryos of a periodic strain of *W. bancrofti* in *Culex fatigans* In the conditions of these experiments the average numbers of larvae found per mosquito decreased from 48.7 at 16½ days after feeding, to 8.8 at 30½ days, the loss indicating the number that left the mosquitoes by the proboscis At 16½ days there is considerable migration from the thorax to the abdomen, and 2 days later the larvae leave the abdomen for the head and proboscis After 18½ days the larvae

begin to escape from the proboscis but this escape may be independent of feeding, for instance where the proboscis contains 5 larvae or more.

HENRARD *et al.* (p. 103) show that *Anopheles f. meatus* and *A. meatus* are easily infected with *W. bancrofti* in the Belgian Congo. *Aedes aegypti* also supports its development but *Culex fatigans* is a poor vector in this area. PERRY (p. 391) has found filarial infection in up to 5% per cent. of *Anopheles farauti* in the New Hebrides and Solomon Islands. HARPER *et al.* (p. 953) state that in the Polynesian islands the vector of *W. bancrofti* is *Aedes pseudoscutellaris* but that in the New Hebrides and Solomon *Anopheles farauti* and (probably) *A. kulensis* are chiefly responsible.

Studies on possible vectors of *W. bancrofti* indigenous to the United States are reported by NEWTON and PRATT (p. 337): three of the mosquitoes examined could be occasional vectors, and two others *Culex pipiens* and *Psorophora discolor* are definitely capable of transmitting the infection under suitable conditions. Development of *W. bancrofti* from the S. Pacific, to advanced or infective stage was found by EVES and MEYER (p. 838) in a number of mosquitoes indigenous to the United States, especially in *Culex pipiens* and *C. fatigans* the latter being the commonest mosquito in the southern States.

GULLIARD (p. 1014) has succeeded for the first time in infecting both *Aedes aegypti* and *Aedes albopictus* with *W. bancrofti*. He discusses the apparent refractoriness of *Aedes aegypti* to *W. bancrofti* in some places, and its susceptibility in others: there seem to be factors of the parasites which vary in adaptability to the vectors.

FRANKS (p. 107) shows that the incidence of microfilariae in the blood is relatively high in persons (on the island of Okinawa) whose blood is of group A.

HIGHBY (p. 446) has shown that the number of microfilariae found per unit volume of blood in the stomachs of mosquitoes is greater (by 7 to 13 times) than the number found in the same volume of blood of the patient on whom the mosquitoes have fed. This is then for a method of concentration which may be useful in diagnosis.

In the course of a paper on intradermal tests for filaria in which an antigen prepared from *Dr. filaris immitis* was used SATAGURS *et al.* (p. 109) make the point that *W. bancrofti* is endemic in the southern United States. With this test they obtained a considerable number of immediate or delayed positive reactions in men from the S. States either with filariasis or who had been in the endemic areas but also in few not so exposed. It appears that infection with any filaria will give a positive reaction but probably not infection with other nematodes. The test is a useful diagnostic aid. WAXTON (p. 834) has used an antigen from *Dr. filaris immitis* in a skin test for filariasis in British Guiana, and finds it positive in almost all infected persons. He does not think that the presence of intestinal worms gives rise to false positive reactions, and he notes that patients with lephantiasts and without microfilariae in the blood gave strong reactions.

FRANK (p. 446) has demonstrated two antibodies in persons infected with *W. bancrofti*: one directed against the microfilariae and one against the adult worms. He discusses the possible use of antigen from adult or microfilariae for diagnostic tests.

WARREN (p. 923) has shown that the complement fixing group specific factor common to *D. immitis* and *W. bancrofti* is present in *L. arum* and *Trichinella parva* though the latter not a filaria.

GILLIES *et al.* (p. 647) have examined the plasma antimony concentration and urinary antimony excretion in man during treatment with or without antimonial. The high plasma level of Neothiosovanilic acids that this may be the drug of choice in the treatment of black fever. The latter is usually of trivalent than of pentavalent compounds was observed. CLARKSON *et al.*

(p 924) describe the tests which indicated that Neostibosan and Neostam gave distinct promise of usefulness in *W bancrofti* infections. With Neostibosan, microfilariae disappeared completely from 23 of 35 patients, and did not return even after a long period of observation. Its effect is to kill the adult worms. BROWN and THETFORD (p 338) report appreciable reduction in microfilariae of *W bancrofti* in some patients as a result of daily injections of anthiomaline, there was no obvious difference in the rate of excretion of antimony between those who did and those who did not respond well to the treatment. CULBERTSON and PEARCE (p 229) show that repeated administration of Stibanose (or Solustibosan) to cotton rats will eradicate infection with *Litomosoides carini*, and they urge its trial in man.

WELCH *et al* (p 1015) report on certain members of the group of cyanine dyes which have shown considerable promise in the treatment of *L carini* infections of cotton rats.

OTTO and MAREN (p 1083) have found that certain substituted phenyl arsenoxides are active against adult filariae of cotton rats and dogs, they are experimenting with these in man.

DUBOIS (p 229) reports two cases in which prurigo was associated with infection with *Loa loa*. JOHNSTONE (p 530) gives an account of his own infection with *Loa loa*, noting that the Calabar swellings were frequent in hot weather but rare in cold. Four adult worms were removed at different times from the eye, and after that the Calabar swellings have ceased to occur. No microfilariae were ever found in the blood.

GABATHULER and GABATHULER (p 924) found onchocercal nodules in a considerable proportion of people in a village in eastern Tanganyika, but in comment GARNHAM points out that they did not use the skin-snipping technique. Immature stages of Simuliidae were present in all the streams. BOZICEVICH *et al* (p 669) have used antigens from *Onchocerca volvulus* and other filarial worms, in the diagnosis of onchocerciasis by intradermal and complement fixation tests. The *O volvulus* antigen was more sensitive than any of the others and gave fewer false positive reactions in persons infected with other worms.

RUIZ REYES (p 1015) gives Anthiomaline as an auxiliary to surgical measures in the treatment of onchocerciasis.

In one of the three onchocerciasis areas of Kenya, where *Simulium neavei*, the vector, breeds in limited stretches of two rivers, GARNHAM and McMAHON (p 1084) have succeeded in eradicating the flies, probably permanently, by applying to the rivers emulsions of DDT in oil and water, to produce a DDT concentration of 2 ppm for 30 minutes at intervals of 10-14 days for 6-7 months. This was enough to kill the developing forms of the flies in successive batches, and at length no living flies could be found. Re-establishment of the flies is unlikely. No serious harm was done to other forms of life. The technique adopted is described.

PEEL and CHARDOME (p 339) have found *Microfilaria streptocerca* in chimpanzees in the Belgian Congo and after having examined the adult worms, have assigned them to the genus *Dipetalonema*.

In an enquiry into *Dracunculus medinensis* infection in a village in the Deccan India LINDBERG (p 925) shows that step wells are apparently more dangerous than curb wells, though the latter are also associated with many infections. Infection was rare under the age of 4, but rose to 85 per cent at age 30-35, after which it fell. Most infected persons had only one or two worms but one had 50. In most cases the head of the worm appeared below the knee. The chief intermediate host was *Thermocyclops vermicifer*. The same author (p 925) shows that incidence is high in Jodhpur where the inhabitants depend on rain water collecting in shallow depressions. The period of onset

is highest between May and September. High temperature is an important factor for the development of larvae in the intermediate host.

SHARMA and HUSAIN (p. 737) report on infection of dogs, in India, with *Dracunculus medinensis*.

WHARTON (p. 106) has successfully transplanted adult *Leishmanosoides carinii* from infected to uninfected cotton rats. SCOTT (p. 447) describes the infection of cotton rats with the filaria *Leishmanosoides carinii* by the bite of *Lapomyia lasota*. He (p. 839) describes a technique for quantitative infection of the cotton rats with larvae removed from the mites by teasing, and injected into the cotton rats by syringe. With his colleagues (p. 840) he describes the technique of rearing the mites.

*Enterobius infection*.—SWELLENGREBEL and SCHLIFFNER (p. 448) have proved that eggs of *Enterobius vermicularis* at least 3 days old, can infect and that if in any patient further infection can be prevented, the worms cease to be passed out after a relatively short time and the infection dies out. The difficulty in practice is that infection from fingers and from materials is so difficult to prevent. The authors discuss treatment.

BIJLMER (p. 111) reports a case in which very large numbers of immature *E. vermicularis* were found in the tissues of the rectal wall of a man who died from gangrenous ulceration of the small and large intestine. The worm invasion was probably a secondary phenomenon.

GELDER (p. 927) has examined *E. vermicularis* (and the comparable *P. salinus amblyopus* of the rabbit) obtained from various parts of the large intestine in relation to the stage of development of the eggs they contain. He concludes that these worms cannot multiply in the intestine without being discharged. MADSEN (p. 110-840) thinks that the migration of female *Enterobius vermicularis* out of the anus is determined by the maturation of the eggs in the uterus, and that the worms wander out to lay eggs in batches, periodically at intervals of about one month.

*Trichuris and Trichinella spiralis*.—Experiment in a mental hospital indicated that the treatment of choice for *Trichuris* infections was administration of emetine in enteric-sealed tablets by the mouth. MURRAY *et al.* (p. 938) obtained the best result with 2 grains for 8 days.

WIND (p. 111) describes an outbreak of trichuriasis in Sweden in which 35 of the 37 infected persons were positive to precipitation test. The incubation period was 14-24 days, shorter in some cases. The onset was often acute with oedema of the eyelids, nausea, vomiting, diarrhoea, fever, headache and eosinophilia.

Skin tests with *Trichinella* antigen were not reliable. ROHM (p. 117) describes 5 immunological tests used in this outbreak, of which the most sensitive is the micro-copie precipitation test in which living larvae are placed in suspected serum, forming a precipitate if the serum has immune bodies.

OPPENHEIM *et al.* (p. 449) describe an outbreak of trichuriasis in prisoners of war acquired from uncooked pork; the chief symptoms were weakness, fever, headache, muscle pains, swelling of the eyelids, swelling, nasal tenderness and anorexia. Treatment was symptomatic since the authors do not believe that any anthelmintic will affect adult worms. *Trichinella* could not be found in faeces, gastric contents, spinal fluid or blood. An outbreak of trichuriasis in New York City is described by SUMMERS *et al.* (p. 113); this was due to uncooked pork sausages. The incubation period was from 7 to 35 days. There were no deaths and the authors comment on the relatively low fatality rates in recent years compared with those which occurred in the 19th century. The explanation probably lies in the fact that as a result of improved control measures, the infections have recently been much lighter than before. Symptoms are described, and the point is made that almost all patients had eosinophilia of over 10 per cent. The eosinophil count is the most useful single laboratory test

for trichiniasis—better than precipitin and intradermal tests (which are discussed), and considerably better than biopsy

LEHMENSICK (p 230) has found *Trichinella* in foxes in Germany and suggests that one cycle of human infection may be fox—wild-rat—house-rat—pig—man

PORTWOOD and SANDERS (p 448) have studied the electrophoretic and allergenic properties of fractions of larvae of *Trichinella spiralis*, but the details of this work should be sought in the original

Charles Wilcocks

## RABIES

SORIANO LLERAS, A Nota sobre la rabia en Colombia [Note on Rabies in Colombia] *Repertorio Med y Cirugia* Bogota 1948, Mar, v 3, No 9, 677-8

In the present article—the continuation of a previous paper on the same subject [this *Bulletin*, 1947, v 44, 1029]—the author deals with the occurrence of human rabies in Colombia and with the effect of specific treatment thereon

Unfortunately certain of the statistics are inaccurately presented and greatly lessen the value of an otherwise informative contribution The following, for example, are difficult of reconciliation

(a) of the 125 deaths from human rabies during the six years 1940-45, there were 54 (43·2 per cent) among bitten persons, who had received complete courses of treatment with SEIPLE's carbolized fixed virus vaccine and 71 (56·8 per cent) among those who had had no treatment or but few injections,

(b) the numbers of deaths from human rabies in the period 1940-45 were, beginning with 1940 25, 26, 29, 17, 20 and 12, i.e. a total of 129,

(c) of the 38,625 bitten persons treated between 1940 and 1945 there succumbed to rabies 129 or 0·34 per cent

On the other hand it seems clear that of 3,023 bitten persons, who during the four years period 1942-45 had received full treatment, only 38 or 1·26 per cent developed rabies This result is held to establish the protective value of the vaccine in use on the ground that according to the estimate of the Pasteur Institute, Paris, 16 per cent of persons bitten by rabid animals and remaining without vaccine treatment fall victim to rabies

It is noteworthy that in Colombia the shortest incubation period of rabies observed in man was 6 days, the longest 5 months [In nature it is seldom under 10 days]

The annual number of cases of human rabies in Colombia shows that the problem is much more serious there than in many other American countries, in the neighbouring countries of Ecuador and Venezuela, for instance, human cases are rare [In the United States cases of human rabies totalled 143 in 1890 averaged 63 annually between 1910 and 1920, numbered 105 in 1928 and thereafter declined In Canada human cases are rare]

G Stuart

LILOU, Y C & KOLO C C Premier cas chinois de maladie d'Aujeszky [First Case of Aujeszky's Disease in China] *Ann Inst Pasteur* 1948, Feb, v 74, No 2, 130-33

In this paper the authors describe the first occurrence in China of the condition known as Aujeszky's disease (pseudo-rabies 'mad itch')

The following paragraphs summarize the clinical manifestations in the affected animal—a cat belonging to a Shanghai family—and the laboratory findings on which diagnosis was finally based

**Clinical history**—The disease commenced suddenly and ran its fatal course in early January 1947. Between the 5th and 7th the cat had recurrent attacks of vomiting and diarrhoea. On the 7th, profuse salivation and anxious expression were noted. On the 8th there was paresis of the hind legs. On the night of the 8th-9th, the cat died. The clinical diagnosis made by an experienced veterinarian was rabies. On this diagnosis two persons bitten while handling the animal, sought anti-rabies treatment.

**Laboratory Investigations**—(a) **Histopathological examination**.—On section, Ammon's horn showed neurophagy, perivascular infiltration with leucocytes, eosinophilic cell inclusions resembling Negri bodies in size and shape, smaller red-staining bodies situated extracellularly and within capillaries.

(b) **Inoculation experiments**.—Material from the medulla introduced into rabbits produced intense itching as principal symptom and death in short space of time after the intracerebral inoculation death occurred in from 24 to 60 hours and after scarification on the shaven skin, in 5 days. Moreover in the rabbit inoculated by the skin route a spinal ganglion showed, on section, the cytological changes described by HENRY as characteristic in Ajazsky's disease: disappearance of the basal substance, eosinophilic staining of the protoplasm, invasion of the nucleus by acidophilic granules and alteration in or loss of the nucleolus.

The authors consider the death of the cat to have been due to Ajazsky's disease and base their diagnosis on the following points:

(a) Although the cat during its illness did not appear to have suffered from "mad itch" nevertheless rabbits inoculated with its medulla showed intense pruritus as a prominent symptom.

(b) Although on section of the cat's brain, cell inclusions resembling Negri bodies were found in Ammon's horn such finding is not frequent in the brains of normal cats.

(c) Neurophagy and perivascular infiltration are more marked in Ajazsky's disease than in rabies.

(d) The incubation period in intracerebrally inoculated rabbits was of very short duration (1-3 days).

(e) The histopathological examination of a spinal ganglion removed from a rabbit which had been inoculated by the scarification method and had died in 5 days revealed a cytology described by HENRY (this Bulletin 1934: 31-146) as characteristic of AJAZSKY'S disease.

[The diagnosis is further supported by clinical signs in the affected cat: abrupt onset and rapid development of illness, profuse salivation and short paralytic stage soon before death.]

G. Smart

RELIOVA, R. V. The Efficacy of our Local Anti-Rabies Vaccine. *J. Philippine Med.* 4: 1948, Mar. 4: No. 3: 129-33. 1 graph.

The anti-rabies vaccine prepared by the Department of Health laboratories at Manila consists of a 1 per cent suspension of fixed virus goat brain and spinal cord in distilled water containing 0.5 per cent phenol. Such prepared suspension is kept in the refrigerator for 5 or 6 months before use.

In the paper under review the author presents experimental proof of the vaccine's efficacy—its antigenicity as determined by the HENRY mouse test, being invariably in excess of the National Institute of Health minimum requirement for anti-rabies vaccines on sale at 1,000 MLD protection.

G. Smart



## MALARIA

MONACI, V. L'esacerbazione dell'endemia malarica e l'anofelismo nel territorio di Venezia [Increase of Malaria Endemicity and of Anopheline Prevalence in the Neighbourhood of Venice] *Riv di Malarologia* 1947, Aug., v 26, No. 4, 191-211, 1 map & 1 chart English summary (9 lines)

After an epidemic of malaria in 1929 in which 10,084 cases were reported in the Venice Province the incidence of the disease declined rapidly. The annual number of cases reported in that province in each of the four years 1937-1940 approximated 2,400. Thereafter there was a greatly increased prevalence, 4,730 cases in 1941, 9,286, 12,105, 13,772 and 11,233 in the succeeding years to 1945. From July 1943 to August 1944, the author carried out an anopheline survey of the area. Catching stations were established, both dwelling houses and stables, at distances of one kilometre along the courses of the Rivers Livenza-morta, Sile, Lemene, Piave nuovo and Gorgonze and the Canale di valle. Estimations of the saline content of waters were also made. *A. sacharovi* and three races of *A. maculipennis* were found, *messeae*, *maculipennis* and *melanoon*. *A. sacharovi* was found where endemic malaria was most severe.

Norman White

DE NEGRI, U. Sorgenti metanifere e malaria nel Polesine (Nota preventiva) [Marsh Gas Borings and Malaria in Polesine] *Riv di Malarologia* 1946, Dec., v 25, No. 6, 217-23, 1 fig & 1 map

In 1934 the sinking of a bore in the Donada Commune of the Province of Venice, with the object of finding a supply of drinking water, failed in its purpose but disclosed the presence of marsh gas, methane, at a depth of 124 metres, and of still greater quantities at 265 metres. Subsequent exploration revealed the abundance of this source of methane and the possibility of utilizing the gas for industrial purposes. The abundance of the gas, the growing demands of industry and the scarcity of fuel occasioned by the war resulted in large-scale developments. At the present time there are more than 60 centres of exploitation each of them containing a number of bores, up to 20 to 25 in some cases. Their depth varies from 200 to 300 metres. More than half the total of more than three hundred bore-holes are situated in the Po Delta.

With the gas is a gush of a large quantity of water having a saline content of from 14 to 24 per cent NaCl. This has resulted in raising the saline content of near-by collections of water making them more favourable for the breeding of *A. sacharovi*, the most formidable vector of malaria in this part of Italy. Thus arose an important factor determining the markedly increased prevalence of malaria that characterized the war years. Other operative factors were the dispersal of population caused by the dangers of bombing, the artificial flooding of certain areas for purposes of defence, neglect of maintenance of canals, reduced antimalaria staff, scarcity of larvicides, and reduced resistance of the population occasioned by malnutrition, etc.

The elimination of the malaria hazard caused by methane bores should not be difficult. The salt water could be drained through pipes to discharge in water courses of sufficient volume to reduce the salinity to an insignificant level.

Norman White

to 60 in Cokloco and in Haute Mana et Haut Approuague respectively. Parasite rates run more or less parallel from 5 per cent. in St. Laurent-du Maroni, 6 in Cayenne to 48 per cent. in Cokloco.

*P. falciparum* is everywhere more prevalent than *P. vivax*. This is interesting in view of the fact that in 1917 Marcel Leger reported that 68 per cent. of all infections were due to *P. vivax* and only 28 per cent. to *P. falciparum*. Over a period of 8 recent years positive blood examinations have revealed the presence of *P. falciparum* in 81 per cent., *P. vivax* in 17 per cent. and *P. malariae* in 1.5 per cent.

Gametocyte indices, Ross's endemic indices and splenometric indices are calculated for each region. They all show that Cokloco, Corossou and Haute Mana and Haut Approuague are highly malarious; most of the coastal communities are also very malarious, Iracoubo, Regina, Sinnamary, Koumou, St.-Georges Ouanary and Mana. Endemicity is very low in Cayenne, Saint Laurent and in the Souvenir area. Malaria is likewise but little prevalent among the Galibi Indians of the villages of Conachi and Iracoubo.

The annual epidemic of malaria in French Guiana occurs in the dry season. Twenty-one species of *Anopheles* have been identified in French Guiana. *A. darlingi* constituted 91 per cent. of the total captured in houses. Its season of greatest prevalence, June to August, is the epidemic malaria season. *A. gyesalis* accounted for 48 per cent. of the captures outside human dwellings.

Norma White

CATILLO R. Répartition du paludisme en Equateur. [Distribution of Malaria in Ecuador.] *Bull. Soc. Path. Exot.* 1918, v. 41, No. 12, 25-31.

The author gives a general account of the malaria problem of Ecuador.

The country is divided into three clearly defined zones. Along the west coast is a region of low-lying plain. The most important anophelines are *An. maculipes* and the population is highly infected with malaria. Transmission occurs in the six rainy months, and particularly at the end of this period when rivers dry up and leave chains of pools. The second zone lies between the two main chains of the Andes. The altitude is about 3,000 ft. and it is said that mosquitoes occur up to 8,000 ft. but the upper limit of native malaria is not stated. In this zone the principal vector is *Anopheles pseudopunctipennis* *s. adleri*. It occurs in both valleys, presumably at a considerable altitude. In a part of this zone the valley of Chillos the insect has been completely eradicated (method not stated). The malaria in this zone in the Andes is clinically malarial.

The third zone lies to the east of the mountains in the upper part of the Amazon basin. There are very large marshes and to the east one descends into a moist equatorial climate. Important vectors are *Anopheles (Kertessia) darlingi* and *An. tritaeniorhynchus* in water holding plants (Bromeliads). In the marshes *A. darlingi* is the prevalent vector.

All parts of the country are malarious and the disease is a major problem in many areas.

J. F. B. White

CRADET A. Aspectos del problema malarial mundial, medios para su solución en la Costa del Perú. Aspects of World Malaria. Means of dealing with the Malaria Problem in the Coast of Peru. Publicaciones de la Dirección General de Salud Pública. Departamento de Malaria. 1947. 41 p. 11 figs.

ALLIS E. I. Food and Malaria. *Amer. J. Trop. Med.* 1948 May. 4, 349-356. 2 parts.

A general discussion.



Twenty-six patients were treated with chloroquine—nine had acute relapses within 3 months. One relapsed 7 months and one 9 months after treatment. Eleven other patients complained of slight symptoms suggestive of relapse but self-medication was responsible for negative blood findings. The total failure rate was 84 per cent—similar to the rate following mepacrine treatment.

Of 63 patients treated with quinine-pamaquin who were followed from 6 to 1 months none showed a laboratory relapse but 18 stated that they had had symptoms suggestive of an attack of malaria. No laboratory relapses occurred among 40 other patients followed for less than 6 months.

The authors found that in the treatment of acute malaria relapses and for suppressive therapy chloroquine was as effective as mepacrine—moreover it was better tolerated and does not have the yellow-dye discoloration effect of mepacrine. It is, however, no more effective than mepacrine in preventing relapses. Quinine and pamaquin combined, under controlled observation and restricted activity of the patient afford a safe and effective means of reducing the relapse rate.

Norman H. Ait

ADRIKARI V. H. Suppressive Mepacrine Treatment to the Staff of B.A. Railway in 1945. *Indian J. Malariology* 1947 June v 1 No. 337-43 2 graphs.

During the malaria transmission season of 1945 and for one month after an attempt was made to give one tablet of mepacrine a day to each employee of the Bengal Asam Railway. This demanded an organisation of considerable magnitude for the staff numbered some 48,000 in 135 stations. In areas where *A. maculatus* was the carrier the administration extended from April to November inclusive. In *A. ph. ph. maculatus* areas the drug was given from June to January. The results appear to have been highly satisfactory. There was a very considerable reduction in malaria incidence and general sickness rates as compared with previous years. Not a single case of blackwater fever was encountered in previous years several cases occurred. No death from cerebral malaria was recorded.

Norman White

MAIER J. Quinacrine Levels in Plasma of Persons with Infectious Jaundice during and after Suppressive Malaria Therapy. *Am. J. Trop. Med.* 1948, May 28, No. 3 395-d.

The plasma level of quinacrine during its administration for the suppression of malaria, and the rate of disappearance of the drug from the plasma after the treatment was stopped, were normal in patients with infectious hepatitis.

LAKSHI S. C. Paludrine in Malaria—Clinical Observations. *J. India Med. Ass.* 1947 Nov. v 17 No. 2, 27-32.

The author reports on the treatment with paludrine of 36 patients suffering from acute malaria. There were 31 *P. m.* and 5 *P. falc. parvum* infections. The results were comparable to those obtained with adequate doses of mepacrine. No toxic effects were noted. One-day single-dose method of treatment is not considered satisfactory. The dosage found satisfactory by the author was 0.2 gm. twice daily for 4 or 5 days and then one similar or smaller dose daily until a total of 3 gm. had been taken.

Norman White

VISWANATHAN D. K. & BAILY J. D. Experiments with Paludrine in the Chemotherapy of Malaria. *Indian J. Malariology* 1947 June 1 No. 2, 307-28.

These observations were carried out in the Bombay Presidency. In Ahmedabad, Vasapur and Belgaum the study was confined to the jail populations.

In the two former places malaria is moderately endemic, the transmission season extending from September to January, Belgaum has little indigenous malaria. Some observations were also carried out in a few villages in the Kanara District where malaria is hyperendemic. The results are recorded in great detail. It was found that paludrine in weekly doses of 100 mgm for adults, 50 mgm for children aged 5 to 12 and 25 mgm for children aged 2 to 4 gave satisfactory results as a clinical prophylactic. These doses were not absolutely effective however, and their administration twice weekly is recommended. A single dose of 300 mgm effects clinical cure in all three forms of infection. Gametocyte production continues after clinical relief and the disappearance of asexual parasites from the peripheral blood after 8 weekly doses of 100 mgm the gametocytes show degenerative morphological changes. In rural areas, clinical prophylaxis with weekly doses is not practicable, but for the treatment of clinical attacks in such areas paludrine, 300 mgm in single doses, is most valuable (smaller doses for children). Tablets might safely be left in the hands of lay village officers for distribution. *Norman White*

MULLICK, K B & GUPTA J C Intravenous Paludrine in Malaria *Indian Med Gaz* 1947, Nov, v 82, No 11, 666-8

The authors report the use of intravenous injections of a solution of paludrine in the treatment of malaria. The solution was made in bulk. 50 gm were dissolved in 2,500 cc of normal saline. The solution was left in a tall jar for 24 hours. The clear supernatant fluid was siphoned off and autoclaved for 30 minutes under 20 lb pressure. 15 cc were injected intravenously.

There were no immediate reactions in any of the 50 patients so treated. In only five cases was a second injection called for. This was given on the following day. Four patients complained of anorexia and 3 of insomnia but it was not possible to determine whether paludrine was responsible for these symptoms. *Norman White*

CHOU, T Q, FU, F Y & KAO, Y S Antimalarial Constituents of Chinese Drug, Ch'ang Shan, *Dichroa febrifuga* Lour *J Amer Chem Soc* 1948 May, v 70 No 5, 1765-7

"From the Chinese drug Ch'ang Shan identified as *Dichroa febrifuga* Lour, there have been isolated umbelliferon, 4-quinazolone, a base with the composition  $C_{18}H_{23}O_3N_3$  and a water soluble alkaloid named dichroine. The last compound has the composition  $C_{16}H_{21}O_3N_3$  and undergoes easily isomeric change with the formation of three isomerides which are provisionally named  $\alpha$ -  $\beta$ - and  $\gamma$ -dichroines, being convertible into each other under suitable conditions. Regarding their antimalarial activity, the  $\gamma$ -isomeride shows the greatest, and the  $\alpha$ -isomeride the least. Based on the results of oxidation and alkaline hydrolysis dichroine appears to be composed of 4-quinazolone and a pyrole derivative which requires further investigation. Dichroine forms both normal and acid salts and a nitroso compound. The isolation of 4-quinazolone from a natural plant, Ch ang Shan, affords a remarkable coincidence with the chemical research for antimalarials along this line." [See also this *Bulletin*, 1948, v 45, 578]

CASTANA, V & MILANI-COMPARETTI, P Studi sulla splenoriduzione nella malaria con sympatol e adrenalina [Reduction of Splenomegaly of Malaria with Sympatol and Adrenaline] *Riv di Malarologia* 1947, June, v 26, No 3 137-52 [16 refs] English summary (5 lines)

The authors report on the treatment of 72 patients suffering from malaria by a modified Ascoli method. sympatol was used in place of adrenaline. The

Intravenous injections were associated with the administration of the usual antimalarial drugs. Sympatol was shown to be preferable to adrenaline in all respects. It was easier to administer the immediate symptoms following injection pallor tachycardia, the feeling of constriction in the chest headache etc. were much less marked and more transient with sympatol the constriction of the spleen was more prolonged the number of injections necessary is much less than the thirty daily injections of adrenaline in graduated doses, advocated by Ascoli. In most cases, 6 or 7 intravenous injections of sympatol were sufficient to obtain comparable results. Only in exceptional cases, in which the reduction of splenomegaly was delayed or incomplete were 8, 10 or 12 injections required.

Norman White

HENRY A. F. V. *Prémunothérapie catalytique du paludisme subaigu et du paludisme chronique. Parasitolyse partielle et hémochromatophénol.* [Catalytic Premunotherapy of Subacute and of Chronic Malaria.] *Revue de Malariologie* 1947 June v 24, No 3 115-36. (Refs. in footnotes.)

Sufferers from subacute or chronic malaria and patients who, through stress of circumstances, have lost their state of premunition to malaria derive the utmost benefit from undergoing a cure in certain hydromineral establishments such as that of Encausse les Thermes (Haute Garonne) if that cure be reinforced by appropriate chemical treatment. The state of premunition may be very rapidly regained. The treatment appears to exercise a catalytic action on all the bodily forces, various glands and the reticulo-endothelial system. In an endeavour to find other means of modifying the interaction of host and parasite the author turned his attention to autohaemotherapy. He has evolved a method of treatment for which he claims great success.

The chronic malaria patient is given preliminary treatment—a daily injection of from 0.8 to 1.0 gm. of quinine for 3 days, and 3 tablets of premaline on each of the two succeeding days. Two days after this treatment some 50 to 70 cc. of blood are withdrawn. The blood is added to distilled water 10 cc. like 1 to 50 cc. distilled water (The blood should give a clearly positive melanofluorescence test and contain no parasite in thick smears). The blood in distilled water is left at room temperature for 7 or 8 hours and then placed in a refrigerator till the following day. It is then centrifuged, the clear red fluid decanted and placed in graduated bottles. Carbolic thionine is then added, 0.5 cc. to 40 cc. of haemolysed blood solution (thionine 1 gm. carbolic acid 8 gm. water 100 gm.) After mixing well it is left for 4 hours. Saline solution, 15 per cent is then added in amount equal to one-quarter of the volume of the haemochromatic fluid. Carbolic acid 5 per cent is added to the saline solution before mixing, the amount being one-tenth of the combined volume of saline and haemochromatic solutions. A final centrifugation completes the preparation, which the name haemochromatophenol is given.

Haemochromatophenol is administered subcutaneously the dose for an adult is 30 cc. An injection is given on each of three successive days, the first being given 36 hours after the withdrawal of blood. Three or four days after the third injection, a fourth and last injection is given. In most cases one series of injections is sufficient. In cases with very large splenomegaly a second series may be necessary when the whole process is repeated.

Spectacular results have been obtained—a notable catalysis of the curative activity. The author discusses at considerable length the possible contribution of each of the various elements of the treatment to the success achieved.

Norman White

HEILBRON I The Role of Chemistry in combating Tropical Diseases *Nature*  
1948, June 19 956-60

A review of modern work on chemotherapy and insect control in malaria and trypanosomiasis

COVELL, G Bats, Clover, Water Lettuce and Malaria *Indian J Malariology*  
1947, June, v 1, No 2, 243-51 [27 refs]

This paper deals with three theories concerned with the prevention of malaria that have received wide publicity from time to time in the lay press None of them has stood the test of serious investigation

Bats as potential destroyers of mosquitoes on a large scale came into prominence in 1909 as a result of the advocacy of Dr Campbell of Texas Attempts to turn his observations and claims to practical account have invariably failed, but his ideas have had recent adherents

The suggestion that clover might have antimalarial properties originated from d'Herelle He thus explained the absence of malaria from areas in which clover is abundant He suggested that coumarin ingested by the female mosquito from clover might inhibit the development of the malaria parasite Investigation has shown that clover has no effect on the incidence of malaria, but d'Herelle's theory has recently received influential advocacy

The water lettuce (*Pistia stratiotes*) according to Dr Roy of Murshidabad, Bengal, was always present in local water collections in his district wherever malaria was prevalent and absent from all healthy areas The removal of the weed from highly malarious villages had completely eradicated malaria Investigation has conclusively shown that Dr Roy's theory is untenable

The lesson to be learned from all this is epitomized in the dictum of Darwin which heads this paper "The most hazardous of human tendencies is the drawing of general conclusions from limited experience" *Norman White*

INDIAN J MALARIOLOGY 1947, June, v 1, No 2, 253-77 Report of a Committee convened for the Co-ordination of Policy regarding the Prevention of Malarial Conditions produced during the Construction of Roads and Railways [COTTER, E, Chairman]

A Committee composed of engineers and malariologists considered memoranda dealing with features in railway and road construction that are likely to create conditions favouring the incidence of malaria, and with the measures that might be taken to prevent such conditions from arising These memoranda are reproduced as appendices to this paper The Committee recommended that the provision of culvert openings under railway and road banks should be more liberal than is the existing practice and should be sufficient to provide for periodic heavy rainfall Culverts should be so designed that a lowering of the invert levels by approximately 5 feet could be effected, if required, without endangering the stability of the structure Borrowpits should be prohibited in built-up areas and for half a mile from their limits Elsewhere, if earth cannot be obtained from another source, specifications are laid down for the construction of borrowpits Adequate provision for their drainage into a natural drainage channel should be made Interconnecting drains between borrowpits should be at least five feet wide, their margins should be kept straight Particular care is required regarding the siting and depth of borrowpits in hilly country on account of the danger of tapping seepage outcrops Adequate drainage should be provided for quarry-pits and cuttings wherever these expose seepage outcrops Measures for the protection against malaria of all persons engaged in railway and road construction should be enforced these measures are

detailed. All engineering projects should make provision for necessary anti-malaria works—a definite proportion of the cost should be earmarked for this purpose.

Norman H. Hill

SKRZCZAK P. La campagna antimalarica con il D D T nel 1946 nelle provincie venete. Antimalaria Campaign with DDT in 1946 in the Provinces of Veneto. *Riv di Malariaologia* 1947 Aug v 28 No. 4 163-82, maps (1 folding) & 6 charts. English summary

There was a large increase in the incidence of malaria in the Veneto Provinces during the war years. 20,629 cases were reported in 1944-45 as compared with 4,669 in 1938-39. In 1946, I. V. R. R. A. collaborated with the Health Department in a DDT campaign. The greater part of the three most malarious provinces, Rovigo, Venice and Udine, were treated. A 5 per cent. solution of DDT was used for spraying. Some 16,000 houses containing 193,000 rooms were treated between May 6th and August 9th. The malaria morbidity was 50 per cent. lower than in the previous year. Primary malaria infections numbered 1,687 compared with 4,443 during the same period of 1945. The 1946 figure includes cases from some areas that were not treated.

Norman H. Hill

LIVADAS C. A. BELIOS G. D. KOROGLIANAKI P. & VALLA C. Results of Malaria Control Activities in Greece during 1946 on Basis of Epidemiological Data. *Arch d'Hygène* Athens 1947 Apr-Dec, Nos. 4/12, 113-24.

The large-scale anti-malaria campaign with DDT carried out in Greece in 1946 has been described previously (this *Bulletin* 1946, v 45 492). On the conclusion of that work an extensive survey was carried out in Epirus, Continental Greece, Peloponnese and the Islands with the object of ascertaining the results achieved. This report gives the result of that survey. In the above areas 5,833 school children were examined to determine the parasite index and 3,910 to determine the spleen index. Blood smears were also taken from 295 babies born between the close of the 1945 malaria season and the autumn of 1946. Of the 90 surveyed areas, 79 had been protected during the 1946 malaria season, in 55 with DDT spray against adult mosquitoes only and in 24 with DDT spray combined with larva control by ground method. Some of the 79 areas also protected by the air-spray programme in nearby swamps. Most surveyed areas were small villages. For the findings in 37 protected areas data of previous years served as a basis of comparison. In these the spleen rates averaged little more than half the previous rates recorded. The parasite rates in 58 protected areas averaged 2.1 per cent. compared with 20.6 per cent., the average of previous recorded rates. In 3 non-protected areas the parasite rates were higher than previously recorded rates. Of 281 babies examined in 28 of the protected areas only one was found infected.

The Malaria Control Service Laboratory in Salonika reported remarkable decrease in the number of positive blood smears. Amongst Malaria morbidity in the army also showed a remarkable decline compared with previous years.

Norman H. Hill

LIVADAS, G. A. Malaria Control in Greece during 1947. *Arch d'Hygène* Athens. 1947 Apr-Dec, Nos. 4/12, 129-33.

The successful DDT anti-malarial campaign in Greece in 1946 provided experience that was turned to profitable account in 1947. The spraying of houses and outbuildings was started on March 15 and by the end of July 4,617 villages with a population of 2,260,500 had been treated. For houses



an emulsion prepared by mixing one part of a 26 per cent oil solution of DDT with 5 parts of water was used, in the previous year 4 to 5 per cent oil solutions of DDT had been used. This change in the preparation used excited much adverse criticism. For some unexplained reason the house fly was much more prevalent in 1947 than in the previous year, though the control of anophelines and other insect pests appeared to be quite as effective with the emulsion as with the oil solution of DDT. Experiments regarding the resistance of flies to DDT are being undertaken.

The population under protection by the house spray method and larva control with DDT amounted to 4,236 500

Norman White

HUDSON, J. H. Land Ownership and Anti-Malaria Law in Malaya. *J Trop Med & Hyg* 1948 Feb, v 51 No 2, 33-40 2 figs

BISHOP, E. L. & HINMAN, E. H. Malaria Control Trends on Impounded Waters of the Tennessee Valley. *J National Malaria Soc* 1948, Mar, v 7, No 1, 12-22, 3 figs

In the south-eastern United States the construction of reservoirs results in an increased anophelism which in the past has caused sharp increases in malaria, the vector mosquito being *Anopheles quadrimaculatus*. A system of tributary and main river reservoirs reaches from the headwaters to the mouth of the Tennessee River and drains a basin on which more rain falls than in any area of similar size in the United States, the shore line of these reservoirs exceeds 10,000 miles in length. The production of electric power and flood control are the main objectives of this extensive water project.

Based on wide experience, regulations for malaria control purposes govern the impounding of water and have for their main objective naturalistic or biological control of the vector mosquito by the development of a clear water surface. This entails careful preliminary attention to malaria control measures in the "blue-print" stage so that such measures may be "built in" or form part of the construction scheme, provision must be made for the raising or lowering of water levels. Lastly an effective shoreline maintenance is essential. Water-level manipulation is now so well understood and applied that, together with shoreline improvements, conditions are so unfavourable for mosquito breeding as to bring very much nearer the time when repetitive measures, such as the application of larvicides, may be almost dispensed with.

In the course of reservoir construction the adjustment of the shoreline involves such work as embankment construction, drainage (with or without pumping) of shallow-water areas, and major filling and deepening operations. Where such methods of control are impracticable or uneconomical, recourse is made to the exclusion of human habitations from the area.

After construction is completed, water level management provides control of both mosquitoes and the vegetation which supports their development. This degree of control is attained by a four-phase variation of water level —

1 Late winter or early spring is flood time and the water level is brought to maximum elevation for the purpose of stranding the winter's accumulation of floating debris.

2 From the commencement of new spring growth until the beginning of production of *A. quadrimaculatus*, a constant high level is maintained to prevent the invasion of the mosquito season shoreline levels by fresh vegetation.

3 For some four or five weeks of moderate *A. quadrimaculatus* production, a weekly fluctuation of level operates.

4 The season of heavy *A. quadrimaculatus* production is associated with a seasonal or summer recession of the water levels. The weekly fluctuation

(1 foot) is maintained and in combination with the steady seasonal fall (1 foot per week) the low level of each successive fluctuation cycle results in the water being drawn sufficiently far out of the advancing vegetation growth to ensure adequate control of *A. quadrimaculatus*.

Shoreline maintenance and improvement including control of vegetation by mechanical removal or the use of herbicides, enhances the effect of water level fluctuation. Where larvicides are necessary DDT as an aerosol or fine spray applied by aeroplane has replaced Paris green. DDT applied as a residual insecticide to all buildings and in particular to animal and human habitations, gives greater protection to the population than routine gassing of dwellings.

The progress in the methods referred to above has resulted in a substantial decline in malaria incidence among the populations adjoining the reservoirs of the Tennessee Valley Authority. Malaria prevention better describes the status of the work than does malaria control.

[This paper emphasizes the importance of including the engineering aspects of malaria control measures in the preliminary planning of reservoir construction. In the development of Africa, water projects may well be followed by the intensive malaria associated with *A. gambiae* and *A. f. nebulosus* unless similar measures to those of the Tennessee Valley Authority are applied from the beginning of construction. The whole project has now been described in detail in book form (see below p. 822).]

R. Ford Tiedie

GARTRELL F. E. & KILMER, C. C. Experience with Use of Permanent Works for the Control of Anophelines on Impounded Water. J. National Malaria Soc. 1948 Mar v 7 No. 1 44-58, 6 figs.

This paper gives in considerable detail with explanatory diagrams the engineering aspects of the malaria control programme for the Kentucky Reservoir of the Tennessee Valley Authority, namely, the drying and dewatering, the filling and deepening associated with the adjustment of the shore line of the reservoir. It does not lend itself to abstraction and should be read in the original.

R. Ford Tiedie

MCCARTLEY R. H. FAY R. W. & SIMMONS, S. W. The Importance of Coverage in DDT Residual House Spraying for Control of *Anopheles quadrimaculatus* Mosquitoes. Pub. Health Rep. Wash. 1948 Mar 24, v 63 No. 13 401-404, 1 fig.

The experiments were done to investigate the importance of thoroughness in application of residual sprays for mosquito control, with the object of determining whether a time-saving spot treatment could be safely employed. A series of bedrooms were chosen and divided into three groups of three. In one set only the predictable resting places of mosquitoes were sprayed, i.e. underbeds of furniture and pictures, the parts of walls immediately behind them, the corner of rooms and the angles between walls and ceilings (representing about 40 per cent coverage). In another set of three rooms the furniture was removed before spraying and only the walls and ceilings (as in routine jobs) were treated (representing 80 per cent coverage). In the final three rooms, both procedures were adopted (100 per cent coverage).

The insecticide used throughout was a 5 per cent aqueous emulsion of DDT. It was applied with an air pressure hand sprayer to give a residue of about 240 mgm DDT per sq ft. Testing was done after intervals of three to six and sixteen weeks by releasing about 500 laboratory-bred mosquitoes from a cage into each closed room and counting rates of knock-down. The species employed was *A. phaeus quadrimaculatus*.



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R. Ford T. Cole

GARTSKILL F. E. & HARRIS, C. C. Experience with Use of Permanent Works for the Control of Anophelines on Impounded Water. *J. National Malaria Soc.* 1948 Mar v 7 No. 1 44-58 6 figs.

This paper gives in considerable detail with explanatory diagrams the engineering aspects of the malaria control programme for the Kentucky Reservoir of the Tennessee Valley Authority, namely the dike, and draw ring, the filling and deepening associated with the adjustment of the shore line of the reservoir. It does not lend itself to abstraction and should be read in the original.

R. Ford T. Cole

MCCAULEY R. H., FAY R. W. & SIMMONS S. W. The Importance of Coverage in DDT Residual House Spraying for Control of *Anopheles quadrimaculatus* Mosquitoes. *Publ. Health Rep. Wash.* 1948 Mar 28, v 63 No. 13 401-7 1 fig.

The experiments were done to investigate the importance of thoroughness in application of residual sprays for mosquito control, with the object of determining whether a time-saving "spot" treatment could be safely employed. A series of bedrooms were chosen and divided into three groups of three. In one set only the predictable resting places of mosquitoes were sprayed (under beds, under clothes, furniture and pictures, the parts of walls immediately behind them, the corners of rooms and the angles between walls and ceilings (representing about 40 per cent. coverage)). In another set of three rooms the furniture was removed before spraying, and only the walls and ceilings (as in routine job) were treated (representing 60 per cent. coverage). In the final three rooms, both procedures were adopted (100 per cent. coverage).

The insecticide used throughout was a 5 per cent. aqueous emulsion of DDT. It was applied with an air pressure hand sprayer at a residue of about 200 mgm DDT per sq. ft. Testing was done after intervals of three, ten and sixteen weeks by releasing about 500 laboratory-bred mosquitoes from each, into each closed room and counting the number of knock-downs. The species employed was *A. quadrimaculatus*.



HERR C. G. & COLLIER F. A Search for the Pre-Erythrocytic Stages of *Plasmodium mex* and of *P. cynomagi*. *J. Parasitology* 1947 Dec., 33 No. 6 Section 2 (Supp.) 27

Following upon their successful in estimation of the development of avian malaria parasites (this Bulletin 1945 v. 4, 5, 8) the authors made an intensive search for pre-erythrocytic stages of *Plasmodium mex* in human volunteers. Salivary glands from infected *Impatiens quadrimaculatus* were inoculated in minimum quantities of fluid into the skin, lymph glands, muscle and isolated organs of the volunteers, and biopsies were made of the inoculated areas. No pre-erythrocytic stages were found in biopsies from 3 areas of skin, 7 lymph glands, 4 veins and 1 piece of muscle, although remnants of the inoculum were usually identified. The biopsies were taken in 7 to 150 hours, but mostly at 24, 48 and 72 hours.

Biopsies of the inoculated areas were subinoculated or grafted into other volunteers in an attempt to demonstrate viable parasites. Infections developed in all the original recipients of parasites but none in those receiving the biopsied areas of skin.

As pre-erythrocytic stages of some avian malaria parasites will develop in hosts which do not have parasitaemia, attempts were made to find such stages in the areas of inoculation of sporozoites of *P. mex*—these were made in liver, spleen, bone marrow and skin of 5 pecked of monkeys, without success. The monkeys in question were *Macaca mulatta*, *Cer. pithecius arctus*, *Cer. pithecius a. pygerythrus*, *Cercopithecus fuliginosus* and *Papio papio*.

Negative results were also obtained in the case of similar experiments with *Plasmodium cynomagi* and the host *Macaca mulatta* at approximately 24, 48 and 72 hour intervals in specimens of liver, spleen, bone marrow and skin.

H. J. O. D. BURKS-Gifford

i. SHORTT H. E. & GARMAN, P. C. C. The Pre-Erythrocytic Development of *Plasmodium cynomagi* and *Plasmodium mex*. *Trans. Roy. Soc. Trop. Med. Hyg.* 1948, May v. 41 No. 2, 785-85 12 coloured figs. on 2 pls. (20 refs.)

ii. ——— & ——— The Exoerythrocytic Parasites of *Plasmodium cynomagi* (Demonstration). *Idid.* 1948 (Dance vol. 713-16)

i. In a series of earlier notes (this Bulletin 1944, 45 Nos 46, 47) and in a demonstration of pictures at a meeting of the Royal Society of Tropical Medicine and Hygiene on 1 February 1948, the senior author and his co-workers have described and demonstrated the pre-erythrocytic schizogony of *Plasmodium cynomagi* in the liver of monkeys and of *P. mex* in the liver of man. In the paper under review a turn is made to the subject and a fuller description of the experiments on monkeys and man is given. Two facts showed that the view that parasites directly entered red blood corpuscles was incorrect. The first was the remarkable difference between blood-inoculation infections and those produced by parasites. In the former case there is no actual incubation period, as parasites appear quickly in the blood, whereas in the latter there is a definite incubation period during which blood inoculated to clean host is non-infective for some days the actual period varying with the species of parasite. At the end of this incubation period the blood becomes infective and soon afterwards parasites are demonstrable in the blood. The second fact is the difference in the action of drugs on the blood and parasite-produced infections. In blood infections antimalarial drugs may completely retard the infection, while in sporozoite-produced infections the parasites will make their appearance sooner or later in spite of drug. Researchers on

## Malaria

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avian malaria have explained these anomalies by demonstrating the existence and nature of the tissue phase and it became obvious that a similar phase must exist in human malaria. Some observers have actually included it prematurely in descriptions of this cycle of human malarial parasites.

In the experiments, large numbers of *Anopheles maculipennis atroparvus* were fed once, twice or three times on monkeys showing numerous gametocytes in the blood. They were then kept at 25° to 27°C at a relative humidity of over 80 per cent and on a diet of raisins or cane sugar. After a suitable time they were then fed on a clean animal and after feeding they were ground in a mortar in heparinized monkey plasma diluted with an equal volume of normal saline solution. The suspension was then inoculated intraperitoneally or intramuscularly or in both ways into the same monkey. The feeding of the mosquitoes on the monkeys was carried out by anaesthetizing the animals with nembutal and placing them in the cage. The anaesthetic effect lasted 1 to 2 hours, during which the mosquitoes could feed without interruption. The animals so infected were examined frequently, so that the infection could be on the liver. This could be repeated frequently, or a biopsy was performed followed in the same animal. Haemorrhage from the cut surface of the liver was easily controlled by cautery. For fixation of tissues, many fixatives were tried but the best results were given by SHORTT and COOPER (*Trans Roy Soc Trop Med & Hyg*, 1948, v 41, 427)\* was used for staining, the Giemsa method described by SHORTT and COOPER (*Trans Roy Soc Trop Med & Hyg*, 1948, v 41, 427)\* was used.

The authors describe one of their monkey experiments and the only human experiment.

In the monkey experiment about 1,000 mosquitoes were infected with *P. cynomolgi* by three successive feeds on a gametocyte-carrying monkey. Ten days after the last feed dissection of 20 mosquitoes showed that all were infected. The surviving mosquitoes, 576 in number, were allowed to feed on a monkey. Over 500 fed. The entire batch of mosquitoes was then ground in a mortar and half the suspension was inoculated intraperitoneally and the

\*The authors' description is as follows —

This method has the advantage of staining cells and protozoal parasites in tissue sections with colour effects resembling those seen in dry smears stained in Giemsa stain. Details of the technique are as follows —

- 1 Fix in Zenker formol-saline or other suitable fixative
- 2 Embed in paraffin wax and cut thin sections
- 3 Remove wax with xylol
- 4 Remove xylol with alcohol
- 5 Bring down to tap water
- 6 \*Treat section with 5 c.c. Lugol's iodine added to 30 c.c. distilled water
- 7 Transfer to 95 per cent alcohol
- 8 Bring down to tap water
- 9 Treat with 0.5 per cent sodium hyposulphite for 10 minutes
- 10 Wash in tap water for 5 minutes
- 11 Stain for 1 hour or longer in Giemsa stain 10 c.c., acetone 10 c.c. methyl alcohol, 10 c.c., buffered distilled water, 100 c.c. (pH 7.2 to 7.4)
- 12 Wash momentarily in tap water
- 13 Differentiate in colophonium resin, 15 grammes acetone 100 c.c. for solution as film forms
- 14 Wash in acetone, 70 c.c. xylol 30 c.c., with several changes
- 15 Apply xylol without draining slide, then apply several fresh changes of xylol until section becomes clear
- 16 Mount in green euparal

\*In the case of tissues fixed in non-mercurial fixatives steps 6 to 10 may be omitted

remaining half in two portions into the thigh muscles. Seven days later the monkey was killed and tissues were removed for examination. So far tissue stages have been found only in the liver.

In the human experiment 3,000 mosquitoes were infected with parasites by two successive feeds on a gametocyte-carrier and the mosquitoes were kept at 24-26°C. at a relative humidity of 5-60 and were fed on rabbits. Fourteen days after the last infecting feed the survivors, 2,010 were fed on the volunteer (A.C.) on two successive days. In addition the salivary glands of 200 were dissected in Locke's fluid and were inoculated intravenously. Seven days later a biopsy was performed on the liver to secure if possible parasites of six or seven day development.

In the *P. cynopteri* experiments the earliest forms were seen on the 5th day and the succeeding stages day by day have been found up to the 10th day. The 5th-day stage is a spherical body measuring 10  $\mu$ . It has a blue or mottled cytoplasm and purple or magenta-coloured chromatin in irregular masses. The masses followed in serial sections number about 50. The outline of the schizont is clear-cut and stands out in sharp contrast with the cytoplasm of the liver cell. The nucleus of this cell is eccentric, owing to pressure of the parasite, but as a rule is not deformed at this stage while the staining of the cytoplasm and nucleus is faint red.

The 6th-day stage is ovoid and measures 18  $\mu$  in longest diameter and contains over 100 nuclear masses. The smooth contour of the parasite at all stages, and whatever its shape, would appear to indicate some kind of pellicle but if this is present it is too fine to be apparent. In some sections the parasite is shrunken leaving a clear space between it and the cytoplasm of the containing cell.

The 7th-day stage is generally ovoid, measuring 31  $\mu$  in longest diameter. In some forms the outline is irregular owing to pressure of trabecular structures such as fibrous tissue or larger vessels. Some have one or more knob-like arms. The parasites frequently show one or more vacuoles, which may be merely sections across indentations. The cytoplasm is coarsely granular and has a pastel-blue colour. The chromatin masses are magenta colour and are numerous and fairly uniformly distributed. From serial sections they number from 600 to 1,000.

The 8th-day schizonts resemble the 7th-day form but there is some indication in smear preparations of condensation of cytoplasm round the nuclei. The 9th-day schizonts show some increase in size with average diameter of 15  $\mu$ . Some forms 45  $\mu$  are encountered.

The 10th-day stage shows considerable change as merozoite formation is complete. Three stages are detectable. In the first, the mature schizont contains merozoites which are kept together by the limiting membrane. Similar forms may be seen on the 9th day. In the next stage the membrane has ruptured and the merozoites are scattered in the surrounding tissues. Each merozoite, consisting of cytoplasm and chromatin measures 11  $\mu$  in diameter. With this rupture of the schizont there is an immediate invasion of the parasitic area by phagocytic cells which engulf numbers of the merozoites but some escape and invade the red blood corpuscles. The third stage represents an invasion in the invading cells—monocytoid cell, polymorphonuclear cell and some plasma cells—which bring about the complete disappearance of the merozoites. These areas of infiltration by cells stand out in the otherwise normal liver tissue. Presumably the phagocytic cells eventually disappear and the area assumes its normal appearance.

In the *P. cynopteri* experiment forms of the 10th and 7th day were found in the liver. The smallest forms seen corresponded with the 5th day form in the monkey experiment but they are larger being about 4  $\mu$  in diameter. The



number of chromatin masses was estimated at 800. Some larger forms were encountered and in some there was indication of microzoite formation. In staining reaction, variations in shape, vacuolation and absence of tissue response, the development corresponded with that of *P. cynomolgi*. One form appeared to represent a rupture of a fully developed schizont and the escape of merozoites. It is not clear whether this is a natural rupture or a mechanical damage to a nearly mature schizont. The merozoites were smaller than those of *P. cynomolgi* and it was not possible to distinguish any cytoplasm. The assumption is made that the rupture was premature. The human subject had been subjected to malaria therapy 22½ months earlier with the same strain of *P. vivax* (Madagascar strain) induced by blood inoculation and had experienced 13 peaks of fever. When the examination of the liver revealed the schizonts it was expected that clinical malaria with parasites in the blood would develop about the 9th or 10th day. In fact there was no clinical attack beyond a transitory rise in temperature on the 15th day, and no parasites were demonstrated in the blood at any time.

In the discussion of these results it is pointed out that the work has provided a solution to the problem of pre-erythrocytic schizogony in mammalian malaria. The *P. vivax* experiment presents an interesting study in immunity. The immunity conferred by the first infection was sufficient to prevent the development of a blood infection, but insufficient to hinder the development of the sporozoites in the liver. There is evidence that a cellular reaction is responsible for the suppression of the blood infection in the invasion of the schizonts of *P. cynomolgi* by phagocytic cells. In fact in the human liver many foci of cell infiltration, often a quarter of a millimetre in diameter, were present. These were not associated with parasites but they probably represented the final attack on pre-erythrocytic forms.

The above account of the pre-erythrocytic development of *P. cynomolgi* commences with a schizont on the 5th day. The complete development is reached on the 8th to the 10th day. The question is raised as to whether the sporozoite requires five days to grow to the size of the 5th-day schizont or whether more than one cycle occurs. While more than one cycle before the fifth day cannot be ruled out, it is assumed that it takes the sporozoite five days to grow to the size of the 5th day schizont. Another unsettled point is the repetition of the schizogony in the liver by merozoites which enter liver cells rather than red blood corpuscles. In avian malaria two types of tissue schizogony occur. One gives rise to small merozoites—micromerozoites—and the other to larger merozoites—macromerozoites. The former are supposed to enter red blood corpuscles while the latter enter cells of the reticulo endothelial system to maintain the exoerythrocytic cycle. The present investigations on *P. cynomolgi* and *P. vivax* have not supplied an answer to these questions. A feature of these liver infections probably explains the failure of other observers to discover the pre-erythrocytic cycle, for HUFF & COULSTON [above], Mammalian Malaria Enquiry [this *Bulletin*, 1947, v. 44, 966], SHORTT, GARNHAM and MALAMOS [*ibid.* 1948, v. 45, 388], and HAWKING, PERRY and THURSTON [*ibid.* 1948, v. 45, 685], failed to produce infections by the inoculation of suspensions of liver taken from animals in the incubation period.

The paper is illustrated by two coloured plates containing 10 figures of the pre-erythrocytic schizonts of *P. cynomolgi* and 2 figures of the pre-erythrocytic schizonts of *P. vivax*. These show very clearly the process of development described.

11 In the account of the Demonstration the main features of the development of *P. cynomolgi* are described and reference is made to other work on mammalian malarial parasites. The largest of these is *Hepatocystes (Plasmodium) kochi*, which also develops in the parenchyma cells of the liver to schizonts 2 mm. in diameter. It is noted that the earlier stages of this parasite are indistinguishable

short a period. The method would appear to provide a useful screening test for prophylactic activity in human malaria as well as for investigating the mechanism of drug action.

J. D. FULTON

TALLAFERRO W. H. & TALLAFERRO LUCY G. Reduction in Immunity in Chicken Malaria following Treatment with Nitrogen Mustard. *J. Infect. Dis.* 1948 Jan. Feb., v 82, No. 1 5-3) 8 figs. [15 refs.]

The authors have previously shown [this *Bulletin* 1948, v 43, 629] that in the case of *P. gallinaceum* and *P. lophurae* infections, exposure to large doses of X-rays may at times reduce immunity possibly through action on lymphocytes and reduction of the amount of antibody formed. The results then obtained have now been compared with those in the same infections in which tri-(3-chloroethyl)-amine hydrochloride (nitrogen mustard)  $\text{N}(\text{CH}_2\text{CH}_2\text{CH}_2\text{Cl})_3\text{HCl}$  was administered. This substance is known to be toxic to lymphocytes and to cause leucopenia, while other nitrogen mustards affect antibody production. The experimental techniques were similar to those employed earlier. The drug was always freshly prepared and was better tolerated by younger than by older birds. One batch of 28 chickens was treated with nitrogen mustard two days previous to and on the day of inoculation with 10,000 blood forms of *P. gallinaceum* while 14 other chickens served as controls. Development of parasites was similar in both groups, but at the peak of parasitaemia infection was more intense in the treated birds. This result was not due to a higher reproduction rate as indicated by the number of merozoites per segmenter or to speeding up of the normal 36-hour asexual cycle which was somewhat asynchronous. A similar experiment confirmed that the infection in treated chickens was more intense but not more lethal.

In chickens treated with the drug 68 to 100 hours after infection, the rate of reproduction was curtailed at one period through reduction in the number of merozoites and all stages of the parasite appeared to be affected adversely. When nitrogen mustard was administered at different stages of the infection after dosage with quinine on the 5th and 6th day following inoculation, given with the object of allowing immunity to develop, the parasitaemia was much more intense than in the control birds. This result appeared to arise from the reduced number of deaths and not from an increase in the reproduction rate. Nitrogen mustard chiefly damaged the parasitocidal mechanism of acquired immunity. Large doses of drug injured both host and parasite. In the control infections there was a wide variation in the number of merozoites produced per segmenter according to the stage of infection.

When nitrogen mustard was given before inoculation with *P. lophurae* the infections were in general more intense than in the controls. The increased intensity of infection in the case of those receiving the largest doses of drug was not due to increased rate of reproduction and the length of the asexual cycle was unaltered. The greater intensity of infection in birds treated in the prepatent period was likewise not due to increase in the number of merozoites or to a speed-up in the rate of reproduction, but rather to a decrease in the immune reaction of the host. When treatment was given in the patent period the merozoites were reduced in number and the infection was partially suppressed. Differences as well as similarities were apparent in the results obtained on treatment of the two species of parasite. In both cases the drug had a brief parasitocidal effect best seen when it was given during the acute rise of the infection and more marked in *P. lophurae* than in *P. gallinaceum*. A lowering of the immunity of the host as evidenced by an increase in parasitaemia and decrease in death rate if the parasite was the most pronounced

effect produced by the drug and probably arises from the destructive action of the nitrogen mustard on lymphocytes and indirectly by reducing the production of immune bodies

J D Fulton

YOELI, M Antigen common to *Plasmodium* and *Haemoproteus* *Amer J Trop Med* 1948, May, v 28, No 3, 387-93, 2 figs

" 1 Complement fixation tests were carried out in a group of 146 pigeons  
" 2 Positive reactions were obtained in all pigeons with a microscopically diagnosed *H. columbae* infection and in the majority of latent chronic infections The complement fixation test particularly with *P. gallinaceum* antigen was found to be more reliable than direct blood examination for the diagnosis of *H. columbae*

" 3 Antigens prepared from *P. gallinaceum* and *H. columbae* gave specific and group reactions

" 4 The existence of serological cross reactions between the genus *Plasmodium* and the genus *Haemoproteus* was demonstrated

" 5 These results are significant in the light of recent findings of primary tissue forms in *Plasmodium*

REDMOND, W B The Electric Charge of Red Blood Cells in Malaria *Science* 1948, Feb 20, 199-200, 1 fig

The surface charge on red cells of the blood is stated to be affected in various processes such as agglutination, phagocytosis and inflammation and the author suggests that penetration of red cells by malaria parasites also affects their electrokinetic charge BROWN [this *Bulletin*, 1933, v 30, 830, 1934, v 31, 352], using the blood of canaries infected with *P. relictum*, found that the charge was reduced during the patent period, and for some time after the disappearance of parasites Infected and non-infected cells migrated at the same rate The factors responsible for the reduction in charge were apparently present in the serum The present electrophoretic experiments, in which the cells were suspended in buffered glucose at pH 7.5, were carried out with normal pigeon blood and during infection of pigeons with *P. relictum* In general it was found that as the infection progressed the electrophoretic mobility of the red cells was reduced and even more so after the peak of parasitaemia was passed There followed a slight increase in rate during the sub-patent period Uninfected cells as a rule migrated more rapidly than those which were parasitized, especially when the number of parasites was decreasing but exceptions were sometimes noted when parasites were small During infection with *P. relictum* the charge on pigeon cells therefore appears to be reduced, being smaller on infected than on normal cells The permeability of the cell may thus be altered and would affect the metabolic processes of the parasite as well as the action of antimalarial drugs

J D Fulton

HAIBA, M H Plasmodia of Common Egyptian Birds *J Comp Path & Therap* 1948, Apr, v 58, No 2, 81-93, 6 pls & 12 figs

Blood smears were taken from 22 species of Egyptian birds and were then examined for parasites 62 birds showed infections, 40 per cent with plasmodia and 60 per cent with *Haemoproteus* The species of *Plasmodium* comprised *P. praecox* (*relictum*), *cathemerium elongatum*, *rouxi*, *nucleophilum* and *gallinaceum* These are described and a few minor differences from the classical forms are mentioned *P. relictum* was found commonly in sparrows (up to 80 per cent being infected), also in pigeons, finches, etc The incubation period

was 7-8 days. This species differs from *P. cathemerinus* not only in the pigment granules but in relative size. *P. dictum* has schizonts measuring 8.8 to 10  $\mu$  with 8-12 merozoites. *P. cathemerinus* has schizonts up to 11.9  $\mu$  in diameter which produce more than 20 merozoites. The incubation period of the latter species was 4-5 days. *P. onca* showed one unusual feature: some of the rings had a cytoplasmic tail ending in a dot of chromatin (so-called insect net form). The alleged presence of *P. gallinaceum* in a dead fowl of European breed is very difficult to understand. This species is not a primary parasite of the domestic fowl, but of the Indian jungle fowl and the present report requires confirmation before acceptance.

The parasites were studied by subinoculation of citrated blood into healthy birds, but no details are given of the actual transmission experiments. Erythrocytic stages were seen in association with infections with *P. dictum*, *cathemerinus* and *elongatum* in reticuloendothelial cells of the brain, liver, spleen and lung more rarely in the kidney and heart muscle. The presence of *P. longum* in such cells and more remarkable still in nerve cells in the brain, will need further investigation. The photomicrograph itself is not convincing.

*Haemoprocus* gametocytes were observed in sparrows, bee-eaters and finches, a second type in pigeons and a third in the black duck, *Anas rubripes tringa*. The parasite in the duck is stated to be larger and to stain more deeply than forms in other birds and to possess large yellow brown pigment granules grouped at the poles of the parasite. The author names it *H. argus* n. sp.

P. C. C. Garnham

### TRYPANOSOMIASIS

GEAR, H. S. African Tsetse and Trypanosomiasis Problems. The Brazzaville Conference, 1948. *South African Med J* 1948, May 22, v 22, No. 11, 34-41.

The author gives a general account of a conference on tsetse and trypanosomiasis which took place at Brazzaville in French Equatorial Africa in February 1948. It was attended by British, French, Belgian and Portuguese Colonial Administrators and by delegates from Southern Rhodesia and the Union of South Africa. The author remarks that the present is a particularly suitable moment for scientists to take stock of a group of infections of such immense importance in Tropical Africa. It is evident from the text that the author himself was present at the conference. His article gains in value because it is written by a man with a wide public health experience.

Some of the meetings were devoted to chemotherapy and interesting communications were made including material that has not yet been published. It is evident that both among the arsenical and antimonial compounds there are substances with great curative effect and others which are very poisonous as prophylactics. Attention was called to the striking differences in results of therapy of infections with *T. brucei* and gambiense. The view was expressed by FAIRBRIDGE that in *brucei* infections treatment is only effective if it is given within four weeks of the infection.

Two territories reported on organized human settlement as a method for the control of tsetse and trypanosomiasis. In Tanganyika there are many thousands of people settled in an area which was formerly occupied by *G. morsitans*. It has been found necessary to settle the population on a considerable compact area and at such a density as to allow man to occupy all parts of the area. When this is done the frontier between cultivation and bush is definite and as short as it can be and thus reduces the contact between man

and fly At Anchau in Nigeria there is an area about 70 by 10 miles in which sleeping sickness was formerly very severe owing to *G. palpalis* and *tachnoides* Steps were taken to exterminate these flies by a limited degree of waterside clearing and there are now fifty thousand people with many cattle in the area During the course of the work much has been done to improve standards of village life, new crops and better farming methods have been introduced together with greatly improved types of housing and layout of villages It is clear that this use of organized human settlement demands a very good understanding not only of fly and bush but also of local agriculture and the habits of the villager In skilled hands it is evidently valuable and it leads to permanent general improvement

The conference also reviewed a number of other methods for controlling various species of tsetse such as discriminative clearing, the use of new insecticides and the control of game

The conference recommended that a standing scientific committee of experts should be set up to provide for international discussion on the progress of research on tsetse flies and trypanosomiasis The French and Belgian authorities were invited to set up a bureau to collect and disseminate information

The author concludes with the hope that these features may ultimately be integrated with other measures for improving the health of tropical Africa as a whole

P A Buxton

CHORLEY, T W *Glossina pallidipes* Austen attracted by the Scent of Cattle-Dung and Urine (Diptera) *Proc Roy Entom Soc of London* Ser A 1948, Mar 18, v 23, Pts 1/3, 9-11

As the result of much experience in Uganda with several species of *Glossina* the author feels that tsetse flies are guided by their sense of smell more than is generally supposed

He has observed that *G. morsitans* does not congregate in places through which elephants have passed but it does congregate where they have rested, even a day or two previously He has made similar observations with *G. pallidipes* and buffalo he also notices that several species of tsetse flies tend to haunt the places where hippopotomus lie up on shore, which are deep in dung These observations lead the author to his view that *Glossina* of several species haunt places where there is a strong animal smell

Chorley has tested this view experimentally, bringing in quantities of cattle dung to places where there were no cattle, and erecting small shelters to protect it from rain, other shelters without dung were put up as controls When arrangements were made to catch *G. pallidipes* round the several shelters, it was found that the numbers were consistently greater round those in which dung had been placed than round the others the difference could be observed even after six weeks when the observer could no longer detect any smell

P A Buxton

CECCALDI, J, TRINQUIER, E, POCHARD, P & VARGUES, R Resultats du traitement de la trypanosomiose humaine par le compose 70 A ou para-arséno [The Treatment of Human Trypanosomiasis with 70 A] *Bull Soc Path Exot* 1947, v 40, Nos 11/12, 439-44

The authors give details of disappointing trials of *p*-arsenosophenylbutyric acid against *T. gambiense* sleeping sickness [for earlier reports and other references, see Report of Brazzaville Pasteur Institute for 1944 thus *Bulletin*, 1947, v 44, 45, and EAGLE, this *Bulletin*, 1946, v 43, 1017]

Treatment was given intravenously and daily for periods varying from 7 to 21 days, the individual dose being 0.4 mgm. per kgm. in 63 cases, and 0.3 mgm. per kgm. in the remaining 4 of the total number treated. Trypanosomes usually disappeared from the gland juice or blood within 15 minutes of the first injection, but of patients in the lymphatic-blood stage only 2 out of 10 treated for 7 days, and only 17 out of 32 treated for 11 to 20 days, were provisionally cured 6 or 7 months after treatment.

All cases treated in the later stages of infection became worse with only 1 exception, and combined treatment with "para-ars no" and trypanamide in this type of case gave results inferior to those associated with established forms of treatment.

E. M. Lewis

THIAS, L. The Persistence in the Blood Stream of some Compounds related to Suramin. *Biochem. J.* 1948, 4, No. 1 109-116 4 figs. [41 r. 1a.]

It was observed soon after the introduction of Suramin (also known under many other names: Bayer 203, Germanum, Antryptol, Moranyl, etc.) that the drug persisted over long periods in the body as shown by prophylactic action, the trypanocidal effect of the serum of treated animals, and by chemical methods. There does not appear to be any particular tissue which acts as a storage depot, since the concentration in plasma is as high as in tissues. The substance has been shown capable of combining with different types of protein matter. It is possible that it exists as large colloidal particles in solution which prevent easy passage through the kidney glomerulus in the same way as passage is prevented through a colloidal membrane. It seems possible that Suramin bears similarity in structure to a natural polypeptide might undergo hydrolysis to its component parts in the body. Dewar or Worstell (this Bulletin 1944, 43, 831) showed, however, that unlike the parent substance, the product of acid hydrolysis was readily eliminated. Partial hydrolysis may offer an alternative explanation of its persistence in the body. The present author has investigated the persistence in the rabbit of suramin and seven other substances either closely related to it or potential products of its hydrolysis in order to obtain information on the structural features which endow it with its special properties and also to find out whether they are correlated with activity. The persistence shown by possible hydrolytic products should all serve as a guide to whether they are actually formed in the body. The method of estimation of these substances in plasma depends on diazotization and coupling reactions based on methods previously used by the author (ibid. 707). Results in control experiments are averaged approximately 10 per cent. For the purposes of estimation, alkaline hydrolysis for period 18 hours was usually used since normal plasma gave smaller blanks by this procedure than if acid hydrolysis was used. In the biological test about 10 per cent. is injected usually with a 2.5 or 10 per cent. solution (the volume of the drug, in doses of 11.1) in 100 g. rabbit plasma, except two times, at 100 g. and 200 g. treated for all the compounds. The level in plasma of suramin and closely related compounds was still high after 5 days. The least persistent compounds were completely eliminated within a few hours, while the others showed persistence intermediate to that of these two groups. Marked persistence was found to be a characteristic of 4 analogues of high molecular weight having negatively charged sulphonic acids other than the sulphonate end groups. Their proteic activity and persistence were not correlated. The possible hydrolytic products were eliminated rapidly and it was concluded that suramin is resistant to hydrolysis and does not break down.

[This is an interesting paper which should be consulted in the original by those interested in order to appreciate the relationships between the various compounds tested] J D Fulton

See also p 757 HEILBRON, The Rôle of Chemistry in combating Tropical Diseases

TAYLOR, Jane & BECKER, E R Liver Changes in Pantothenate-Deficient Rats infected with *Trypanosoma lewisi*: *J Infect Dis* 1948, Jan-Feb, v 82, No 1, 42-4, 4 figs

Young rats fed on a standard diet deficient in pantothenic acid are capable of developing unusually heavy infections of *T lewisi*, with associated pathological changes. These changes are attributed by the authors to the enhanced parasitaemia rather than to the dietary deficiency, since the latter alone produces only moderate effects. The deficiently fed infected rats weigh much less than normal, with proportionately decreased liver weight, but their spleens become heavier in proportion to body weight to a greater extent than in the case of infected animals fed on a normal diet.

Trypanosomes were found not only in the Kupffer but also in the parenchyma cells of the liver. Agglomerated masses of trypanosomes, which normally appear in infected rats from the 10th to 14th day of infection with *T lewisi*, were not seen in the blood or in organ smears from infected animals fed on the deficient diet. In specimens examined from animals on a normal diet it was noted that these agglomerations were significantly more frequent in liver impression slides than in blood smears. A possible explanation is that the liver sinusoids exercise a screening effect. E M Lourie

ERCOLI, N & WILSON, W Influence of BAL on the Toxicity and Chemotherapeutic Activity of Mapharsen *J Pharm & Exper Therap* 1948, Feb, v 92 No 2 121-6

BAL reduces the toxicity of arsenicals and of certain other metallic compounds. The question therefore arises whether it interferes also with their chemotherapeutic activity, and the authors have investigated this question by experiments in which mice infected with *Trypanosoma equiperdum* were treated concurrently by mapharsen and by BAL.

It was found that BAL does, in fact, interfere substantially with chemotherapeutic activity under these experimental conditions. The interference is greater where the criterion of chemotherapeutic effect is sterilization than where it is mere temporary disappearance of trypanosomes from the circulating blood.

Toxicity to the host is influenced by BAL much less than chemotherapeutic effect, thus, the amount of BAL compared with mapharsen necessary to interfere with toxicity was found to be 1 0-2 7 times as much, whilst doses of BAL as low as  $\frac{1}{4}$  of the mapharsen weight can interfere with the sterilizing (i.e. curative) effect.

The authors conclude that their findings establish the unsuitability of this form of combined chemotherapy. E M Lourie

CHEN, G Effect of Arsenicals and Antimonials on the Activity of Glycolytic Enzymes in Lysed Preparation of *Trypanosoma equiperdum* *J Infect Dis* 1948, May-June, v 82, No 3, 226-30, 3 figs [11 refs]

"Mapharsen, stibamine and tryparsamide were shown to inhibit the activity of hexokinase, adenosine triphosphatase and 3-phosphoglyceraldehyde dehydrogenase systems in lysed *T equiperdum*.

"The inhibition may be antagonized by cysteine."

produced by intraperitoneal inoculation of a suspension of infected spleen, and the disease (which is symptomless in the cotton rat) progressed regularly with no tendency to spontaneous cure. The animals did not die, however and in this way differed from hamsters, which invariably succumb to leishmaniasis. The spleen became enormously enlarged and contained numerous parasites—the liver equally so during the early stages. The infection did not pass to the offspring of diseased mothers. Guinea voles were susceptible.

P. C. C. Garnham

MUNIZ J & MEDINA, H. Leishmaniose tegumentar do cobaiá. *Leishmania curatilis* n. sp. [Cutaneous Leishmaniasis in the Guinea-pig.] *Hospital*. Rio de Janeiro. 1948, Jan. v 33, No 1 7-5, 10 figs. English summary

Since at present, the species of *Leishmania*, *L. curatilis*, with which this article is concerned appears to be almost restricted to the guinea-pig, the subject is one of comparative pathology, mainly and does not call for a very detailed account. The reasons for mentioning it here are that it is a species easily cultivated, that guinea-pigs are readily infected, experimentally as well as spontaneously, and that it may be used for testing therapeutic substances. Subcutaneous inoculation of material from lesions or from cultures invariably sets up the disease in guinea-pigs, but very rarely does so in other animals. Rhesus monkeys, hamsters, dogs, white rats and mice were heavily inoculated but only one hamster (*Cricetus cricetus*) and one puppy showed any leishmanial lesions and they were small and seemed to be regressing. The pig (*Citra sporea*) known also as the Brazilian opossum and closely allied to the guinea-pig, could not be thus infected. Reciprocally the guinea-pig is resistant to infection with *L. tropica* and *L. donovani*. The morphological characters of *L. curatilis* are described in detail.

H. Harold Scott

TORRES, C. M., MUNIZ J., CARDOSO Rita L. de A. & DUARTE, Eitel. Caracteres do granuloma histiocitário na leishmaniose espontânea do cobaiá. [The Histological Characters of Leishmanial Granuloma of the Guinea-pig.] *Hospital*. Rio de Janeiro. 1948, Mar. v 33, No. 3 403-8, 3 figs. English summary

One of the most characteristic features of infection of guinea-pigs by *L. curatilis* is the production of a granuloma consisting largely of histiocytes and macrophages enclosing many of the parasites in their cytoplasm. Equally characteristic are the readiness and rapidity with which these cells become transformed into fibroblasts and may then be diagnosed as fibromata or even more commonly, as spindle-celled sarcomata—pseudo-neoplasms, as the authors designate it (though why pseudo is not clear unless the term neoplasm is restricted to malignant growths). Three photomicrographs show the condition well and from the third it can easily be understood how confusion might arise and a diagnosis of fibro-sarcoma be made.

H. Harold Scott

## FEVERS OF THE TYPHUS GROUP

HAYONEN, M. Clinical and Serologic Observations during a Typhus Fever Epidemic. *Ann. Med. Intern. Fenn.* 1948, 37 No. 1 51-60 (14 refs.)

In one section of a hospital for prisoners of war 32 cases of typhus fever occurred within a period of six weeks. In five of the cases the Weil-Felix reaction remained negative throughout the illness and in all but one of the



remaining cases the reaction became negative within nine weeks of the end of the illness. A positive reaction with the Widal test occurred in 12 cases. The fatality rate was 44 per cent.

*John W D Megaw*

WANG, P J, FU, H H & LIU, W T. A Note on Typhus Fever in Lanchow. *Chinese Med J* 1948, Feb, v 66, No 2, 79-83

During the three years 1943-1945 the authors studied 131 cases of typhus fever at Lanchow in North-West China. The epidemiological conditions pointed to louse-borne infection.

Three strains of rickettsiae were isolated, these caused frequent Neill-Mooser reactions during ten consecutive passages through guinea-pigs but examination of the strains by the USA Typhus Commission workers at Caro showed that they gave complement-fixation and immunity reactions indicating epidemic-typhus infection.

Local house rats and their fleas were examined, but no evidence of infection could be detected.

*John W D Megaw*

DE MAGALHÃES O, ROCHA, A & RODRIGUES, I. Contribuição para o conhecimento do tifo exantemático neotrópico no Brasil. Nota prévia [A Preliminary Note on Epidemic Typhus in Brazil] *Brasil-Médico* 1948, Apr 3 & 10, v 62, Nos 14/15 154-5

DE MAGALHÃES O & ROCHA, A. Contribuição para o conhecimento do tifo exantemático neotrópico no Brasil (Possibilidade da transmissão pelo leite). Nota prévia [A Preliminary Note on the Possibility of the Transmission of Epidemic Typhus by Milk in Brazil] *Brasil-Médico* 1948, Apr 3 & 10, v 62, Nos 14/15 153-4, 1 fig

GIROUD, P & JEZISKI, A. Comportement sur poumon de lapin du mélange du virus aphteux O et des rickettsies du typhus épidémique [The Effect of Lung Inoculation of the Rabbit with a Mixture of the Virus O of Foot-and-Mouth Disease and Epidemic-Typhus Rickettsiae] *C R Soc Biol* 1947, Dec, v 141, Nos 23/24, 1181-2

In the course of their studies of the virus of foot-and-mouth disease the authors carried out experiments on the effect of lung inoculation of rabbits with a mixture of the virus and epidemic-typhus rickettsiae.

By the end of five successive passages the rickettsiae had died out, whereas the virus continued to be transmitted.

*John W D Megaw*

FRANKE, R. Die Weil-Felixsche Reaktion nach Fleckfieberschutzimpfung, [The Weil-Felix Reaction after Anti-Typhus Inoculation] *Klin Woch* 1947, Sept 15, v 24/25, Nos 47/48, 746-9, 1 fig

Weil-Felix tests were carried out on a group of 60 persons before and after inoculation with three doses of yolk-sac, mouse-lung, or rabbit-lung vaccine. Four to five days after the third dose a titre of 1-100 was observed in 50 per cent of the cases, in 10 per cent the titre rose to 1-400, and in two cases it was 1-800. In 10 per cent no rise of titre could be detected. In a few cases the test was repeated three weeks after the last dose of vaccine, and in nearly all of these the titre had fallen to an appreciable degree.

*John W D Megaw*

BLACK T O Employment of Soluble Antigen in Screening Tests for Typhus Complement Fixation. *Pub. Health Rep. Wash.* 1948, Apr 23, v 63, No. 17 529-37 [13 refs.]

Soluble antigens liberated from suspensions of *Rickettsia prowazeki* and *R. mooseri* by ether extraction are known to be incapable of differentiation between epidemic and murine types of infection, but they have great practical advantages over the more specific purified antigens in being easily and cheaply prepared.

The author describes the technique by which he has prepared the soluble antigens from several strains of epidemic and murine rickettsiae. He has employed the strains in complement fixation tests of antisera obtained from guinea-pigs infected with different strains of rickettsiae. The same antisera were also tested with specific purified antigens prepared from the strains of rickettsiae used in the above tests. It was found that soluble antigens prepared from any of the strains of epidemic and murine rickettsiae gave positive reactions with every strain of antiserum and that the reactions were usually at higher titres than those obtained with specific antigens, even when the latter were prepared from homologous strains of rickettsiae.

Further tests were carried out on 475 sera of presumably healthy persons from Korea and Japan. 47 of the sera were anticomplementary. 169 reacted at titres of 1/10 to 1/60 and of these 72 were positive also with epidemic or murine specific antigens or with both. In no case did a serum react with a specific antigen when it had not already reacted with soluble antigens of every strain used in the tests, and in only six cases was the reaction with the soluble antigen at a lower titre than that with the specific antigen.

It was concluded that in diagnostic and survey work a preliminary set of screening tests with soluble antigen, either epidemic or murine, would greatly diminish the number of tests that would have to be carried out by the troublesome and costly employment of the purified specific antisera.

John H. D. U. GAW

HENNER, K. Über die Behandlung des Fleckfiebers. [The Treatment of Typhus Fever] *Min. Woch.* 1947 Nov 1 v 24/25 Nos. 53-54 848-51.

Since 1941 the author has had experience in the treatment of more than 1,000 typhus patients in a large war hospital in the "East."

An analysis is given of the results observed in 900 acute cases seen between October 1941 and March, 1944. Dividing the 900 cases into six equal groups in chronological sequence it was found that the fatality rate showed a remarkable decline. In the first group treated in the winter of 1941-42 the death rate was 38.3, in the next two groups it was 16.7 per cent. and in the last two it had fallen to 6.0 per cent.

The author admits that this striking improvement certainly cannot be attributed solely to better methods of treatment but he claims that his latest system deserves wide publicity because of the remarkably good results that were obtained.

Drugs claimed to be specific including atabrin, plasmoquine, cubain, cibazol and pyramidon, are regarded as useless, sometimes dangerous. Convalescent serum when given after the third day was without value.

The secret of success is claimed to consist in the administration of cardiovascular tonics and sedative drugs when and only when there are indications that these are needed. Threatened vaso-motor collapse is treated by such drugs as camphor, caffeine, strychnine, adrenaline and strophanthin, and by intravenous saline. For severe headache, insomnia and restlessness morphia, luminal and veronal are recommended.

In the winter of 1944, a number of patients who came under treatment on the second or third day were at once given 500 cc of convalescent blood and the results observed are said to have been startling, but little information is given with regard to the number of cases treated or the evidence on which so early a diagnosis was made. The author simply states that the symptoms and circumstances of cases left no room for doubt as to the nature of the illness

John W D Megaw

EHRlich, J, BARTZ, Q R, SMITH, R M & JOSLYN, D A **Chloromycetin, a New Antibiotic from a Soil Actinomycete** *Science* 1947, Oct 31, 417

A *Streptomyces* sp was isolated from a soil sample in a field near Caracas, Venezuela. Agar streak cultures were found to inhibit inocula of numerous common Gram-positive and Gram-negative organisms. Filtrates of submerged aerated cultures of the *Streptomyces* showed marked antibacterial activity against several Gram-negative bacteria, especially *Sh sonnei*. A crystalline antibiotic has been isolated from the filtrates and the name Chloromycetin is proposed for it. Details of preparation are described. The *in vitro* activity of the crystalline product against several bacteria is shown in a table. The intravenous LD<sub>50</sub> for 20 gm mice is 3.0 mgm/mouse. Chloromycetin, unlike streptomycin, appears to be well absorbed when given orally to mice and dogs.

The immediate interest of this new antibiotic to readers of this *Bulletin* lies in its indications of antirickettsial activity [see below]

H J O'D Burke-Gaffney

SMADeL, J E & JACKSON, E B **Chloromycetin, an Antibiotic with Chemotherapeutic Activity in Experimental Rickettsial and Viral Infections** *Science* 1947, Oct 31, 418, 1 fig

The authors describe tests on chick embryos and mice infected with *R orientalis* and have found the drug highly effective. Mice treated with suitable doses either by the intraperitoneal or oral route were completely protected against lethal doses of infection. For example, daily doses of 2.5 cc of the drug given by the intraperitoneal route saved all the eight mice whose treatment was started five days after infection. Daily doses of 5.0 mgm given by the mouth saved seven out of eight mice whose treatment was started two days after infection.

Similar results were obtained with chick embryos infected with *Rickettsia akari* (of rickettsialpox), *R prowazeki*, *R mooseri*, *Dermacentroxenus rickettsi*, and two strains of psittacosis virus. Mice infected with *R akari* were treated with similar success

John W D Megaw

PAYNE, E H, KNAUDT, J A & PALACIOS, S **Treatment of Epidemic Typhus with Chloromycetin** *J Trop Med & Hyg* 1948, Apr, v 51, No 4, 68-71, 2 figs & 2 maps

Chloromycetin had already been found effective in preventing the death of embryo chicks infected with various rickettsiae, including *Rickettsia orientalis*, *R prowazeki*, *R mooseri*, and *R rickettsi* [see above]

The authors describe clinical trials of the drug during an epidemic of typhus fever in Bolivia in December, 1947. It is stated that 16 cases of typhus and 'five normal controls' were treated, and that six of the cases were adequately studied and followed up.

The report consists of a description of one fatal "control case," and of six of the treated cases in which all of the patients are said to have shown rapid improvement, resulting in convalescence within three days.

The drug was given orally to four of the patients in doses of 0.5 to 1.0 gm. twice daily for three days, and intravenously to the other two patients, aged 17 and 14 years respectively, in doses of 0.2 and 0.25 gm. twice daily for three days. No toxic reactions were observed.

[Although the results as described do not lend themselves to a definite evaluation of the effects of the drug they justify further trials which, if possible, ought to be carried out in conditions permitting comparison with alternate controls, either untreated or treated with para aminobenzoic acid.]

John W. D. McGraw

RICHARD, E. R. & RILEY, E. G. A State-Wide Survey of Typhus Fever in Florida. *Amer J P & Health*, 1943, Apr v 38, N 4 541-9, 3 charts & 1 map.

The name typhus fever is employed in the title of this paper as a designation for murine typhus. A description is given of a detailed survey of the incidence of the disease in the State of Florida during the three years, 1941-1943.

About 69 per cent. of the population (2,250,000) lived in urban conditions in towns of 1,000 inhabitants and over. The officially reported numbers of cases for the three years were 493, 380 and 420, respectively, but the real numbers were estimated as being at least 1,234, 1,045 and 793. Personal investigations were made in about two-thirds of the cases.

The distribution was comparatively uniform throughout the State, the rural population was nearly as heavily affected as the urban. The incidence was considerably higher among the white than the coloured population and among adults than young children, but the authors believe that many cases occurring in coloured persons and children are likely to have been missed.

During the period, 1,337 cases with positive or doubtful Weil-Felix reports from State and private laboratories were investigated. 1,038 of these had given reactions at titres of 1,320 or over, and in 95 per cent. of this group the diagnosis was considered to be justified on clinical grounds. Among the 299 cases with reactions at a titre of 1:160 the diagnosis was confirmed in 73 per cent.

In 67 per cent. of the cases, infection was believed to have been acquired in the homes; in 28 per cent. places of business were considered responsible, and about two-thirds of these were concerned with food handling; in the remaining cases no opinion could be formed with regard to the place of infection.

There was a sharp decline in the incidence during the period in the two regions in which control measures were being carried out.

John W. D. McGraw

LEON, J. V., MURPHY, J. N. Jr & DAVIS, D. E. The Distribution of Endemic Typhus in Rats in Lavaca County, Texas. *Pub Health Rep Wash*, 1943, May 1 v 63, No. 21 69\*-4.

\* Based on results of complement fixation tests for endemic typhus of rats in Lavaca County, Texas.

"1. Ninety-four percent. of 10 urban establishments sampled harbored rats with positive tests. Of 47 *Rattus attus* from urban establishments, 61 percent. gave positive tests and 134 *Rattus norvegicus* 69 percent. gave positive tests.

"2. In rural or semi-rural areas 77 percent. of 203 farms or semi-rural establishments harbored rats with positive tests, and 44 percent. of 529 rats gave positive tests.

3. The widespread distribution of typhus in rats on farms suggests that such rats must be included in control activities.

# Fevers of the Typhus Group

Vol 45, No 9]

FITZPATRICK, Florence K **Susceptibility to Typhus of Rats on Deficient Diets.**  
*Amer J Pub Health* 1948, May, v 38, No 5, Pt 1, 676-81

Groups of 12 or more rats were kept for six weeks on various diets planned so as to imitate deficiency diets such as exist or might occur in different parts of the world. Then two-thirds of the rats in each group were inoculated intraperitoneally with varying doses of murine-typhus rickettsiae. In some of the experiments the infecting doses were lethal to 50 per cent of normal rats, in others the doses were sublethal.

The susceptibility of the rats was found to be increased by diets deficient only in one of the following respects (1) low proteins, (2) one-tenth of the optimum supply of vitamins of the B group, (3) reduced pantothenic acid, (4) reduced riboflavin, and (5) reduced thiamin.

Rats kept on diets deficient only in containing one-fortieth of the optimum amount of one of the following substances: pyridoxine, choline, nicotinic acid, and para-aminobenzoic acid were not affected. With a similar reduction in the amount of thiamin, pantothenic acid or riboflavin, premature deaths occurred among the rats.

The addition of one per cent liver powder to the complete diet did not increase the resistance of the rats to infection.

An interesting point was that rats kept on a natural laboratory diet were decidedly less susceptible to infection than those kept on a complete synthetic diet, even though the latter caused a greater increase in weight.

Full details of the diets employed and of the results of the experiments are given in the paper.  
*John W D Megaw*

DUNN, T B **A Case of Murine Typhus in London** *Brit Med J* 1948, May 22, 979-80

A Jewish patient aged 61 years, who had emigrated from Western Russia 36 years ago, was attacked by typhus fever in June, 1947.

A fortnight before the onset he had been engaged at the London Docks in testing eggs belonging to a cargo that had arrived from Poland. He said that he had frequently been bitten by fleas while at work. A search was made for rats in the area but none could be found. There was no evidence of louse infestation.

The Weil-Felix (OX19) titre was 1-125 on the 11th day and 1-500 on the 14th day. With the rickettsia-agglutination test, a titre of 1-2,560 was observed with murine rickettsiae and one of 1-640 with epidemic rickettsiae.

Infestation of the egg packing cases with infected fleas was suspected of being the source of infection. In spite of the patient's having lived in Russia till the age of 25, the diagnosis of Brill's disease is regarded as very unlikely. A further report on the serological findings is promised.  
*John W D Megaw*

SAVOOR, S R & DAS MENON, P, in collaboration with S M MERCHANT  
**Scrub Typhus (Tsutsugamushi Disease) in Bombay** *Indian Med Gaz*  
 1948 Dec v 82, No 12, 752-6, 1 fig on pl [13 refs]

Four cases of scrub typhus are described as occurring in persons who had not gone outside the municipal limits of Bombay City during the four weeks preceding the onset of the attacks. In two cases there was an eschar, and in one case *Rickettsia orientalis* was isolated from a patient's blood by mouse inoculation and by intraocular inoculation of rabbits.

The authors think that three of the patients had probably been infected through contact with mite-infected coarse vegetation. In the fourth case the only possible source of infection seemed to be the handling of vegetables.

All the cases occurred during and after the rains (June to December 1945) and in a footnote SOMAN states that he has detected 17 cases of scrub typhus in Bombay during the months September, October and November 1946. *R. orientalis* was isolated from seven of the patients. No cases occurred during the other months of the year although the system of detection was the same throughout the period.

John H. D. Meyer

FINDLAY G. M. & ARCHER, G. T. L. The Occurrence of Tick-borne Typhus in West Africa. *Trans. Roy. Soc. Trop. Med. & Hyg.* 1948, May v 41, No. 6 813-18 1 chart.

Three cases of typhus fever diagnosed on serological evidence as tick-borne occurred during the last three months of 1943. The patients were Europeans living in military camps—two of them were stationed in North Ashanti and appear to have been the persons referred to in a paper by FINDLAY and ELIAS (see this Bulletin 1943, v 45 322)—the third patient was living on the Jos Plateau in North Nigeria.

The chief evidence pointing to tick-borne infection is stated as being the absence of complement-fixing antibodies and agglutinins for murine and epidemic typhus and the presence of antibodies for South African tick typhus. In one case rickettsias were isolated from the patient's blood and passaged twice through guinea-pigs, in which some inflammation of the tunica vaginalis occurred. This patient's blood gave a Weil-Felix reaction with the slide test "against Proteus O1, but not against P OX19 or P OXA—the complement-fixation titre against epidemic and murine antigens was 1-50 against South African tick typhus it was 1-400.

In the other two cases the epidemic and murine titres were 1-50 and 1-10<sup>3</sup> respectively—the tick-typhus titre was 1-200 in each case.

John H. D. Meyer

VILES J. O. & BOCKHE G. C. The Use of Para-Aminobenzoic Acid in a Case of Rocky Mountain Spotted Fever. *New England J. of Med.* 1948 May 27 v 238, No. 22, 60

"A case of Rocky Mountain spotted fever treated successfully with para-aminobenzoic acid is presented. No toxic effect to the drug were noted.

WACHMANN T. Ueber eine Q-Fever (Queenslandfieber)—Epidemie in Graubünden. [An Epidemic of Q Fever in Graubünden (Grisons, Switzerland).] *Schweiz. med. Woch.* 1948, June 5 78 v 22, 529-31 4 figs.

In April 1947 19 cases of Q fever occurred among 75 persons who had been engaged in unpacking and erecting a large printing press which had arrived from Cincinnati, Ohio packed in straw in several wooden packing cases. The work of unpacking and erecting took four days and it was obviously during this period that infection occurred. The average incubation period was estimated as about 10 days, the extreme range was 9-23 days.

The nature of the disease was not recognized till nine months after the occurrence of the outbreak, when complement fixation tests against an American strain of *Rickettsia burnetii* gave positive responses in the 16 patients whose sera were obtainable. The titres ranged from 1-10 to 1-320. The diagnosis in most of the cases had been influenza or fever of uncertain origin.

Infection was believed to have been due to the inhalation of infected dust from the straw contained in the packing cases.

John H. D. Meyer

STRAUSS, E & SULKIN, S E Studies on Q Fever Complement-Fixing Antibodies in Meat Packers at Fort Worth, Texas *Proc Soc Exper Biol & Med* 1948, Feb, v 67, No 2, 139-41 [Refs in footnotes]

Sera from 1,443 persons engaged in handling meat at plants in Fort Worth, Texas, were tested by Bengtson's method for complement-fixing antibodies of *Rickettsia burneti*. Positive reactions at titres of 1-8 or over were obtained in 114 cases (8 per cent), including 17 cases (1.2 per cent) in which the titre was 1-64 or over.

These results were regarded as showing that some unrecognized attacks of Q fever had occurred among the persons examined.

Further studies are in progress to find whether the antibodies occur among persons belonging to other occupational groups in the area.

John W D Megaw

SULKIN, S E & STRAUSS, E Studies on Q Fever Persistence of Complement-Fixing Antibodies after naturally acquired infection *Proc Soc Exper Biol & Med* 1948, Feb, v 67, No 2, 142-4

Sera from 17 persons known to have had naturally acquired attacks of Q fever in March, 1946, at Amarillo, Texas, were tested at later dates for complement-fixing antibodies of Q fever.

All the sera gave positive reactions five to seven weeks after the attacks, in the 11 cases in which the titre was estimated it ranged from 1-64 to 1-1,024.

Among 13 sera tested six months after the attack, 10 gave titres of 1-32 or over, the other three gave titres of 1-16, 1-8, and less than 1-8, respectively.

Seven sera were tested 17 months after the attack, all were positive at titres of 1-16 or over, including one at 1-128 and one at 1-1,024.

It was thought possible that the person who reacted at 1-1,024 may have had "continued contact with the rickettsial agent subsequent to the initial illness."

John W D Megaw

ASCHENBRENNER, R Pathogenetische und therapeutische Probleme beim Wollhynischen Fieber [Pathological and Therapeutic Problems of Trench Fever] *Klin Woch* 1947, May 15, v 24/25, Nos 31/32, 481-8, 7 figs [57 refs]

The paper contains a critical review of the literature dealing with trench fever as observed during the two World Wars, and a brief description of a few cases seen by the author in 1942 and 1943.

Most of the papers discussed have already been reviewed in this *Bulletin*. The author is very sceptical regarding the value of the numerous special lines of treatment that have been recommended by German physicians. He specially condemns the light-hearted use of injections of bacterial toxins and mentions a case of sudden death after an injection of "Pyripher" given intravenously. He also states that another patient died suddenly after an intramuscular injection of prontosil. He states that an independent trial has failed to substantiate the claims made by HESSE and KREMSER for X-ray therapy in chronic cases, but in a later issue of the same journal [see below] Hesse asserts that the author when challenged was unable to produce satisfactory evidence with regard to the nature of the trial.

The paper conveys the impression that surprisingly few additions have been made during the recent war to knowledge of trench fever.

John W D Megaw

- HESSER, E. Pathogenetische und therapeutische Probleme beim Wolbrymchen  
Fieber (Pathological and Therapeutic Problems of Trench Fever) *Ann.*  
*Woch.* 1947 Nov 13 24-5 Nov. 53, 54, 55  
See above

## DENGUE AND ALLIED FEVERS

- PERRY W. J. The Dengue Vector on New Caledonia, the New Hebrides, and the  
Solomon Islands. *Am. J. Trop. Med.* 1948, Mar. v. 28, No. 2, 53-9  
(10 refs.)

It has been known for some years that dengue occurs in those parts of Melanesia to which the paper refers. In this area, *Aedes aegypti* occurs as a relatively recent introduction limited to areas round ports and places where Europeans live. In such places dengue occurred and the author concluded that it was carried by *Aedes aegypti*. He also gave attention to the possibility that it might be carried in completely rural areas by members of the *Aedes scutellaris* group. Of these, *Aedes hebrius* is widely distributed in the area, breeding in small rot holes etc., in the forest and biting man freely. The author could find no evidence of the occurrence of dengue in such areas. As he observes, his experience is different from that of MACNEILAS in New Guinea (see this Bulletin 1947 v. 44 518). In that island, sporadic outbreaks of dengue occurred in rural areas, in the absence of *Aedes aegypti*; the virus was passed through the bite of *Aedes hebrius* to healthy volunteers.

P. I. D. 4104

## PLAGUE

- MALTA. REP. ON HEALTH CONDITIONS OF THE MALTESE ISLANDS AND WORK  
OF MED. & HEALTH DEPT. FOR YEAR 1943. CAVALI, J. Chief Govt. Med.  
Officer. Appendix III. pp. 1571-92. Report on the Outbreak of Plague  
1945-48.

Early in 1945 plague had already appeared in the port of Algiers Oran  
Haifa, Jaffa, Ferryville and the Suez Canal Area, spreading later to Ajaccio  
Tarent, Palermo and Rhodes. In Malta it broke out at the same time as in  
Ajaccio. Altogether 80 cases of bubonic plague made up the epidemic. None  
was pneumonic and only one septicaemic. The epizootic that occurred in rats  
was widespread and human cases were soon recorded from different localities  
with the result that bubonic plague was notified as existent from June 1945.  
The course of the epidemic followed in this report month by month up to  
June 1948 with a total of 22 deaths and case mortality rate of 77.5 per cent.  
Both epidemic and epizootic seem to have subsided, for no infected rats have  
been detected since 1 January 1947. The rat poisons used in combating plague  
were zinc phosphide and arsenic.

W. F. HARTON

- HADDAD, C. & VALEAU, A. Streptomycin in Bubonic Plague. *Brit. Med. J.*  
1948, May 29 1074-7

Three severe cases of treated bubonic plague and one control untreated as  
not a large number. They are published as being sufficiently dramatic to  
suggest that streptomycin is superior to any drug that has preceded it in



regular use In the three cases treated with streptomycin (200 or 300 mgm every 3 hours) both sulphonamides and penicillin had been without effect The administration of streptomycin, however, gave rapid improvement and final recovery The fourth patient, who was not treated with streptomycin, died  
W F Harvey

## CHOLERA

ABDOU, S Susceptibility to Cholera *Lancet* 1948, June 12, 903-4 [18 refs]

The epidemiology of cholera as regards its vibrio, its incidence and its spread, presents many problems for debate Susceptibility and severity are two outstanding problems and these are the subjects treated by the author Cholera "does not strike all classes with the same severity" One Egyptian village of 1,600 inhabitants presented a good example Many of the inhabitants suffered from multiple infections schistosomiasis, ankylostomiasis, amoebiasis, ascariasis and malaria One family group of 150 persons contrasted markedly with the rest, for it was free from parasitic infections and all of them "in spite of their varied economic status" escaped the infection There were 52 cases of cholera in the village with 25 deaths The deaths were distributed—so far as examination proved it—among those suffering from intestinal schistosomiasis or some other parasitization with or without pellagra Eleven deaths out of 21 were in children and these had not been examined for parasites "Anyone over the age of one year who had diarrhoea and vomiting and died within two days" was considered to have had cholera The author pays attention to the pathways of human infection, the oropharyngeal and the gastro-intestinal, and discusses the bearing of gastric acidity on susceptibility, achlorhydria and hypochlorhydria would remove the barrier to passage of vibrios into the intestine Another puzzling circumstance in this village outbreak was, for a disease with the case-to-case reputation of cholera, that seldom more than one member of any household was attacked with cholera "If the vibrio crosses the stomach barrier, its further fate depends on many factors, of which the intestinal pH is perhaps the one that determines the development of disease or of the carrier state, or the destruction of the vibrio" Vaccination was started five days after notification of cholera, but the author concludes that "a high standard of sanitation seemed to be a better safeguard than immunization"  
W F Harvey

## AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

CALVO FONSECA, R La incidencia de la *E histolytica* en Cuba Plan para lograr la uniformidad de los métodos de investigación y técnicas de examen coprológico a usar en las encuestas sobre *E histolytica* en los países Americanos [Incidence of *E histolytica* Infection in Cuba Plan to secure Uniformity of Method in American Countries] *Bol Oficina Sanitaria Panamericana* 1947, Nov-Dec, v 26, Nos 11/12, 943-53 English summary

Records of the incidence of *E histolytica* infection in Cuba have been very contradictory and misleading They have been made in a few, isolated districts and returns have ranged between 1.2 and over 30 per cent Moreover, some observers have classed *histolytica* infections under the general term amoebiasis, not distinguishing this species from *E coli* and *Endolimax nana*

"3. It is suggested that the source of the riboflavin found in the bugs fed on rats deficient in this vitamin is the intracellular symbionts which every bug is known to possess."

PACKCHANI, A. The Fate of *Trypanosoma duttoni* in *Triatoma*. *Ann. J. T. P.* 31 & 1948, May & 28, No. 2, 363-6.

PESA CHAVARRIA, A., SÁENZ HERRERA, C., CORDERO, E. & BOLAXOS, L. Enfermedad de Weil en Costa Rica. Estudio de un brote epidémico en la ciudad de San José [Weil's Disease in Costa Rica. Study of an Outbreak in San José.] *Bolet. Oficina Sanitaria Panamericana* 1947 Nov-Dec, v. 28, Nos. 11/12, 930-68. English summary.

The outbreak investigated occurred in June-August 1944. Sporadic cases, or small groups of cases, had been observed for several years among children but these had been regarded as cases of catarrhal jaundice. The first patient seen in this outbreak was a child, 5 years of age who suddenly became feverish, and irritable and had loss of appetite, headache, intestinal disturbance, albuminuria and, after 4-5 days, jaundice. Leptospirae were seen in the urine. She was discharged from hospital after being ill for a little more than a fortnight. In rapid succession other cases occurred, in adults as well as children, and altogether 34 cases were recorded. In all but one leptospirae were found in the urine or blood and sera agglutinated *L. icterohaemorrhagiae* in dilutions up to 1:5,000 and a few *L. ranicola* up to 1:100 (in one patient 1:200). Rats in the neighbourhood were examined and 31 out of 74 had a blood infection; another 4 per cent showed leptospirae in the urine and 18 per cent in the faeces, 62 per cent positive altogether. Examination of the stomach contents of fleas caught on the rats also revealed leptospirae. It is thought, therefore, that this insect may be a vector of infection. *H. Harold Scott*

## LEPROSY

LEPROSY IN INDIA 1948, Jan. & 20, No. 1 100 pp. Special Issue. All-India Leprosy Conference, Wardha.

This Conference was attended by 74 delegates and a number of politicians. The 100-page report contains little that is new. The first part is taken up with short speeches by politicians from each province and an address by the Director of Health Services, Government of India, and is followed by abstracts of papers and their discussion: these deal with different sections of the work and the resolutions adopted by the Conference. The main part of the report records either in full or in abstract the papers read, such as mentioned in the earlier part but with no reference to the papers when they are recorded, nor are those of the same subject printed together which is an inconvenience to the reader. No list of papers or index is supplied.

The following summarizes the most important points apart from 10 important subjects, which are dealt with separately below.

A discussion on planning of anti-leprosy work follows the usual lines: small colonies for 100 patients near their villages are recommended when a near-by medical man is available. The optimum number for each colony or village considered to be 500. On the question of diet, leprosy control in rural and vagrant homes are suggested for by the Government. The importance of the subject is stressed and the need for distribution is emphasized.

## Leprosy

Vol 45, No 9]

profession Leprosy surveys are considered to be no longer required except as a preliminary to effective anti-leprosy work. In Orissa, a three years' survey of 1,400,000 persons revealed 25,000 cases, about 4,000 of whom were infective.

A long discussion of social and economic aspects of leprosy included full consideration of sterilization of males by vasectomy to prevent children being born to infective parents. This was thought to have a place, but should be a voluntary procedure. The importance of leprosy in children was once more stressed and special institutions for isolating children living with infected persons were advocated by RAMANUJAM (whose paper in summary was presented by COCHRANE), but others thought it better to send them to live with healthy relatives.

As in the case of all recent leprosy conferences much time was expended on reading papers on and discussing the classification of leprosy cases, much to the confusion of most workers on the subject. It was ultimately resolved that it would be unwise to discard completely the Cairo classification, but it should be suitably modified to bring it into line with recent advances. Other resolutions provided for the appointment of an all-India leprosy officer, for more training for leprosy workers and the admission of leprosy cases to general hospitals, it was agreed that home isolation of children is the cheapest method but is not applicable on a wide scale. Further "immediate steps" should be taken to start colonies and group isolation centres in all seriously affected areas. [It is to be hoped that under national government this may be implemented without further delay as a similar resolution was passed at the Calcutta 1920 Leprosy Conference at the reviewer's suggestion with practically no effect, except in Madras in nearly thirty years.] Further propaganda, research and suitable iteration on political grounds of the title Indian Council of the British Empire Leprosy Relief Association were also resolved on.

L Rogers

DHARMENDRA Need for Fresh Anti-Leprosy Legislation in India Leprosy in India 1948 Jan, v 20, No 1, 59-63

COCHRANE, R G Legislation in Leprosy Ibid 91-2 Discussion 25-8

The papers and discussion on this difficult subject are of importance. The first speaker pointed out that, except under a recent Madras Act, the legislation is out of date in not distinguishing between infective and uninfected cases and is ineffective in only applying to urban areas. Compulsion leads to hiding and is only necessary under special conditions. Moreover, all Indian institutions are full, so voluntary isolation must be mainly relied on. Fresh legislation is required as a Model Leprosy Act with notification and compulsory powers only as regards infective cases in which lepra bacilli can be demonstrated, provision for isolation of all such cases (a very large order) including those in the more highly infected rural areas. In highly endemic areas, legal powers should be mandatory and not only permissive with maintenance of places of isolation for infected cases, and powers for Health officers to examine any cases supposed to be infective. Infective persons should be restricted from the use of public vehicles and from engaging in occupations that may endanger others, and infected paupers rendered liable to arrest and removal. Control of immigration of leprosy patients and regulations regarding measures for effective home isolation should be taken. Leprosy workers should be consulted in the framing of the new Act, which is urgently required for circulation to provincial governments before a final draft is enacted.

The second speaker, Cochrane, with experience of the recent Madras legislation, considered that laws which encourage an atmosphere of fear and drive patients into hiding are bad. The majority of infections are in children and young adolescents and only a minority become infective, and they are not equally

dangerous, so only those most likely to come into close contact with leathir persons need be dealt with. It is impracticable and unnecessary to prevent them from travelling in public conveyances except in the case of prolonged close contact in ship cabins. It is also quite impracticable in India to isolate all infective patients and investigation is required to discover the minimum amount of segregation needed to control the disease so it can only be used in limited areas to meet particular and special circumstances and to prove its efficacy.

After a long and discursive discussion it was resolved that existing legislation should be amended in the light of modern knowledge since present legislative measures are of no practical value.

L. Higgs

Smeyers R. D. G. P. Enkele clinische gegevens over een 87 tal lepralidern.  
"Biotrophisme indirecte I pretuse der anti-syphilitische behandeling.  
Photosensibilisatieproef op de na lepra. (Clinical Features. Indirect  
Biotrophism and Photosensitivity Testing in Leprosy) Nederl. Tijdschr  
v Geneesk. 1948, May 29 v 92 (d) No. 22, 181-197 figs. (8 on 1 pl.)  
English summary (8 lines)

Many interesting features of leprosy are recorded in this study of 87 leprosy patients, in whom the diagnostic complications of syphilis and skin diseases were increased by avitaminosis and nutritional disturbances acquired in concentration camps. Leprosy manifested itself in the accepted forms of lepromatous and non-leprosy but the latter showed out only as "basenrudes" (tuberculoid) but also as "intermediate" forms. It is evident that when dealing with the signs of leprosy definition of terms is very necessary and that care must be taken over the significance of terms such as tuberculoid, tubercular, syphilitic and leprosy. The leprosy "macula" also may be a raised patch and not the dermatologists macula.

Among these patients there appeared useful leprosy signs such as madarosis (loss of eyebrows) and leprosy gynecomastia, claw hand and "wager dysphagie". Those doctors who work in leprosy-ridden countries are probably on the look-out for typical and atypical manifestations of leprosy. Two unusual manifestations among many others are described here. The first is cited as a case of indirect leprosy biotrophism. Direct biotrophism is the reaction brought out say in syphilis by a specific provocative dosage; the indirect reaction is that pertaining to some other disease, say a malarial attack which is precipitated by antisyphilitic treatment. In the present instance a 20-year-old patient with primary syphilis, after his ninth injection developed a typical acute leprosy reaction with leonine faces and aching fast bacilli in his nasal mucus. It had evidently been at the same time a case of latent leprosy.

The second case was peculiar: an 18-year-old blonde youth with declared photosensitivity of the skin upon treatment with bergamot oil and exposure to sun. It was a case of nerve leprosy and many of his neurotrophic leprosy skin areas, although devoid of lanugo hair and showing altered pain and temperature sensation, analgesia and thermo-anesthesia, but not touch sensation were immediately relieved by application of bergamot and exposure to the sun. This should have been followed by dermatitis and subsequent darkening of the reaction areas. The leprosy maculae however remained depigmented as vitiliginous leprosy, the areas of analgesia in which, in some cases, were only paresthesia.

The leprosy and tuberculin tests in these leprosy patients followed well known lines.

H. E. Harvey

DHARMENDRA & CHATTERJEE, K R Treatment of Leprosy with the Sulphone Drugs *Leprosy in India* 1948, Jan, v 20, No 1, 71-5 [12 refs]  
Discussion 32-4

This trial was carried out on 50 advanced and lepromin negative lepromatous cases in a Calcutta hospital over a period up to 19 months, during the course of treatment blood changes were watched and a diet with increased proteins and vitamin B was given. Promin, diasone and sulphetrone were administered in the usual doses. The first was found to be too toxic, but the last two given orally proved to be more effective than any other treatment, although slow in their action. Simple estimations of haemoglobin only sufficed to enable consequent anaemia to be combated, because its decline runs parallel to that of the red corpuscles and it is not necessary to estimate the concentration of the drugs in the blood except for research purposes. Only a few of the patients failed to tolerate the treatment. Improvement is seen in the form of subsidence in the extent of large infiltrations and nodules and disappearance of small nodules. Leprotic ulcers, including nasal ones, heal quickly and do not recur, and eye conditions improve. Reactions are checked and become less frequent. On the other hand, bacteriological improvement was not marked and in only two cases did smears become negative although in others the numbers of bacilli were generally less. These drugs had no effect on nerve pains and nerve abscesses, and loss of sensation did not show any improvement. Altogether the effects were less than those described by others and these preparations have definite limitations, but the new treatment is considered to be safe, if the precautions already mentioned are taken. Hydnocarpates, therefore, remain the best routine treatment in the generality of cases and especially in many neural ones.

In the discussion which followed, Cochrane repeated his view that the sulphone drugs should be restricted to experimental trials until more experience is acquired, but in his reply Dharmendra said there was no justification for holding back the use of these drugs by general practitioners so long as the necessary simple blood examinations and other necessary precautions were taken. A. T. ROY advocated giving hydnocarpus oil in a few courses of big doses followed by smaller ones, he considered that this produced the best results.

L. Rogers

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## HELMINTHIASIS

LOVETT-CAMPBELL, A C A Note on Bilharziasis in West African Troops  
*Trans Roy Soc Trop Med & Hyg* 1948, May, v 41, No 6, 821-2, 1 fig

Of 532 military recruits admitted to a hospital in Northern Nigeria in 19 months between 1940 and 1942, 74 had schistosomiasis [this is shown as 18 per cent, but is in fact 13.9 per cent]

*S. haematobium* accounted for 59 cases, *S. mansoni* for 11 and a combination of both for four. One of the last named died. Hookworm and ascarid infections were also present in 60 per cent of the infected group and *P. falciparum*

malaria in 5 per cent. Haemoglobin varied between 65 and 85 per cent and eosinophilia from 8 to 19 per cent. Red cell counts were never below four million per cmm. Treatment was by means of anthelmintic response to this drug alone was slow so a concluding course of sodium antimony tartrate was given in each case.

The men had been medically examined on enlistment and those infested with schistosomes had been either rejected or treated. It is therefore likely that the present infestations were either those overlooked on enlistment or relapses after inadequate treatment had they been new infestations contracted during manoeuvres a much higher percentage would have been expected.

Contrary to a belief held at the beginning of the war that schistosomiasis caused little physical impairment in recruits, infested men soon broke down under prolonged stress. This was especially noticeable on long marches and a distinctive triad of symptoms was common namely backache in the loins, caecal tenderness and mucoid diarrhoea. Where backache predominated vesical lesions tending to encroach on ureteral orifices were seen on cystoscopy. Caecal tenderness indicating large bowel involvement was common in *haematodes* as well as *mansoni* infestations and one soldier had gross *haematodes* lesions in the appendix.

In an endemic area in the Sokoto Province 57 per cent of 35 appendicectomies revealed schistosome infestation. Appendicectomy is usually indicated in schistosomiasis where caecal tenderness remains after specific drug therapy or radiography shows imperfect filling or delayed emptying of a retrocaecal appendix.

H. J. O'D. Burke-Gaffney

MILLER C. V. ROSS W. F. & BLAIR, D. M. The Diagnosis of Rectal Schistosomiasis. *J. Trop. Med. & Hyg.* 1948, Mar. v. 51 No. 5 91-4

A diagnosis of rectal schistosomiasis is usually based on the recovery of ova of the worms from the stools. In S. Rhodesia, where the severer dysenteric form of the disease is rarely seen even serial stool examinations may reveal but an occasional egg. Here in many cases giving a positive intradermal test with a cercarial antigen, eggs cannot be found in the stools but postmortem infection of internal organs can be demonstrated by a potassium hydroxide digestion technique in these cases.

In 1921 FULFORD (*this Bulletin* 1923 v. 20 19) described a concentration technique for the recovery of schistosome ova from stools and the recognition of their presence by hatching. A modification of this method has been employed in S. Rhodesia. In 1943, OTTOLINA and ATENCIO (*ibid.* 1944 v. 41 845) examined the diagnostic results yielded by their puncture and by rectal biopsy in schistosomiasis. GELFAIN (1948 in the Press) is stated to have found rectal biopsy a successful method of diagnosis of schistosomiasis in S. Rhodesia. HERNANDEZ MORALES and MALDONADO (1946) (*ibid.* 1947 v. 44 330) found the biopsy method to give 100 per cent positive result as compared with a 40 per cent result yielded by a 100 concentration technique. KRAUSE and SALAS EL DI (1930) (*ibid.* 1939 v. 27 963) compared the results obtained from direct stool examination from a stool flotation technique and from rectal swabs. Of these the rectal swab method gave the higher number of positive results in rectal schistosomiasis. WALLIN (1947) (*ibid.* 1947 v. 44 529) designed grooved rectal scrapers and by this method detected 61 per cent of cases, while an acid-Trisodium Phosphate faecal concentration technique in Luanda revealed 78 per cent positives.

The authors examined 50 unselected Africans in the Salisbury Native Hospital for rectal schistosomiasis using (1) their cercarial antigen intradermal

test, (2) rectal biopsy, and (3) a Weller's three-grooved scraper as diagnostic procedures. Of these, 41 gave positive intradermal tests, 27 gave positive rectal biopsies, and only 2 were found positive by Weller's scraper technique, 4 were negative as judged by all these tests. A further series of 17 cases was examined by biopsy and by Weller's scraper, 14 of these were shown to be positive by biopsy, but only one with the scraper, this latter was a case not revealed by biopsy. Ten other cases of schistosomiasis with *S. mansoni* ova in the stools were examined by Weller's technique, and from only one of these did the scraper recover eggs.

Weller's scraper therefore proved an unsatisfactory instrument for the detection of rectal schistosomiasis as encountered in S Rhodesia. The reason for Weller's own success in its use may be attributable to the fact that *S. mansoni* infestations are much heavier in Egypt and in the Caribbean area than in S Rhodesia, where diarrhoea, with the passage of blood and mucus, rarely results from them. Furthermore the scraper takes material only from the lowest 9 cm of the bowel, while biopsy yields material from a level about 15 cm up the bowel.

In 5 cases with negative intradermal tests biopsy yielded eggs. Eggs obtained by biopsy are not always viable, in many cases they were seen to be dead and degenerate. Their presence, therefore, while it constitutes residual evidence of an infection, does not necessarily indicate a need for specific treatment. Old-standing cases of rectal schistosomiasis may be self-cured, and specific treatment is necessary only when the eggs are demonstrably viable.

In S Rhodesia, cases of infestation with worms producing terminal-spined ova far outnumber those harbouring *S. mansoni*. The rectal biopsy technique revealed a much higher incidence of terminal-spined egg infestation than did stool examination, Weller's scraper usually failed to reveal intestinal infestations with terminal-spined eggs. It would seem that terminal-spined eggs have difficulty in escaping from the gut wall into the intestinal lumen.

A R D Adams

**MAKAR Bey, N** Two Interesting Cases of Bilharzial Papilloma and Epithelioma  
*J Roy Egyptian Med Ass* 1948, Mar, v 31, No 3, 217-21, 1 coloured fig, 2 photos & 4 microphotos on 6 pls

In the first case, the patient, an Egyptian male of 25, suffered from a large ulcerating cauliflower-like mass which protruded from the anus. He had a past history of intestinal and urinary bilharziasis which had been treated repeatedly. dead schistosome ova were found in the urine and stools, and X-rays showed "bilharziasis of the bladder". A course of tartar emetic was given and the growth was removed later by diathermy in two sittings. The pathological report revealed that the growth showed "the typical structure of bilharzial polyposis". It contained many living and dead ova, but no malignant changes were seen. The author points out that such advanced conditions are not commonly seen nowadays, and he is of the opinion that neither tartar emetic nor any of its substitutes affect the fully developed bilharzial lesion, possibly because of fibrosis obstructing the vascular channels. The advantages of the form of operation employed are discussed.

The second case was that of an Egyptian male of 40, complaining of a warty mass on the inner aspect of the right thigh, below the crease of the groin. It had begun in the form of nodules in the skin three years before. There was a history of haematuria occurring 2 or 3 years before the skin nodules developed. *S. haematobium* ova were present in the urine.

After a course of tartar emetic had been given the mass was excised. Schistosome ova were found in the dermal papillae and superficial currim. Parts of an ulcerated area of the growth were typically epitheliomatous. The patient received radiotherapy and was apparently cured when he left hospital.

The author points to the rarity both of schistosomal lesions in such a site and of the appearance of epitheliomatous changes in them where the skin is not exposed to such irritants as occur when the lesions exist at mucocutaneous outlets.

Because of this rarity and the initial difficulty in diagnosis, the case was at first thought to be one of leishmaniasis with superimposed epitheliomatous changes.

[See also this Bulletin 1947 v 44 101L.] H. J. O. D. Barker, *Queer*

GELFAND M. The Prognosis in Schistosomiasis. *J Trop Med & Hyg* 1949 June v 51 No 6 117-19 [23 refs]

The gravity of schistosomiasis as a cause of disablement and of death among Africans in S. Rhodesia is examined. Digestion of the rectum and of the bladder obtained post mortem from 300 adult natives of Mashonaland showed 94 per cent. to be infected with schistosome ova.

Cirrhosis of the liver occurs in 8 per cent. of Africans, and primary liver carcinoma in 1 per cent. of them although firm ascribed to schistosome infection a similar incidence of these conditions has been reported from schistosome-free areas. The author does not accept schistosomiasis as a cause of liver cirrhosis and believes this to be due to some other factor such as protein deficiency. The liver changes in schistosomiasis are localized around the eggs, there is no alteration in the main hepatic structure or evidence of liver metastasis.

Almost half of the schistomiasis patients had ova in the lungs but pulmonary hypertension and dilatation of the right heart due to pulmonary arteriole stenosis, Myxomatous syndrome and pneumonia and other pulmonary disorders doubtless due to infection were not found at the 300 post mortem examinations, although schistosome infection of the appendix is common and chronic appendicitis at rare times in the Bantu.

Stricture of the ureters with back pressure, hydronephrosis is much less frequent than dilatation of the ureters. Hydronephrosis may be associated with this dilatation owing to impairment of the peristaltic function of the ureter because of its thickening. The back pressure may be augmented by reflux of the urine from the bladder through the incompetent ureteric orifice. Eighty-three (33 per cent.) of 250 cases had gross lesions of the ureters, and of these about 77 per cent. consisted of dilatation alone, only 3 per cent. showed stenosis. Fifteen per cent. of the 83 (5 per cent. of the total cases) had hydronephrosis which was usually associated with ureteral dilatation. Only 1 per cent. was the hydronephrosis responsible for death. Nevertheless, 60 per cent. of those with lesions in the bladder have lesions in the ureters and half of these develop either dilatation or stricture of the ureters. A percentage of these suffer from hydronephrosis which will in some cases ultimately cause death.

Acute inflammatory infections of the urinary tract due to schistomiasis are not clinically common and rarely do they cause death. Stone formation is extremely rarely due to the schistosome parasite. Vesical carcinoma is relatively uncommon, occurring in only one quarter as many cases as primary carcinoma of the liver. Carcinoma of the bladder indeed is less common than in Europeans, in spite of the high incidence of vesical schistosomiasis in the Bantu. The effect of schistosome infection on other organs is problematical. The author



considers that schistosomiasis is not as serious a disease as is claimed in the literature, and that its true gravity is primarily due to its effect on the ureters

- A R D Adams

[Much of this paper deals with schistosomiasis without distinction of species, although the author's observations on lesions of the urinary tract refer specifically to *S haematobium* infections, he does not always indicate which species is concerned in other lesions. He does, however, state that his findings do not bear out the current belief that *S mansoni* has a greater predilection for the liver, and in his own experience he found *S haematobium* ova in the liver in just under 50 per cent of the cases, but those of *S mansoni* in just over 23 per cent. He also quotes SHAW and GHAREEB (this *Bulletin*, 1938, v 35, 665) who conclude that Ayerza's disease may result from either species. In the section dealing with appendicitis, no indication is given of the species of schistosome involved. It is of some importance, in papers dealing with schistosomiasis, that whenever possible the species concerned should be indicated so that subsequent references in the literature may be clearly related to the particular aetiological form of the disease. Ed]

HALAWANI, A, WATSON, J M, NOR EL-DIN, G, HAFEZ, A & DAWOOD, M.  
**Miracil D a New Chemotherapeutic Agent for Bilharziasis** *J Roy. Egyptian Med Ass* 1948, Mar, v 31, No 3, 272-84

Miracil is a new compound, 1 methyl-4-beta-diethyl-amino-ethyl amino-thioxanthone HCl [this *Bulletin*, 1948, v 45, 526]

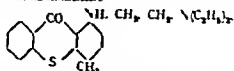
The compound was given orally to 16 patients infected with *S haematobium*, who were subsequently examined at weekly intervals for 2½ months. Ten received total doses of 2 to 5 gm during 5 to 10 days, apart from one very light infection, none of these was cured. Three patients were given 7.5 gm during 8 to 10 days, two were cured and one relapsed. The concentrations of miracil in the blood mostly ranged from 0.12 to 0.37 mgm per 100 ml. In ten cases the drug caused slight increases in the systolic blood pressure and in the pulse rate. Among the symptoms reported by the patients were — giddiness (10 patients), vertigo (1), weakness and inertia (2), headache (2), epigastric pain (2), colic (2). The patient with vertigo suffered severe and repeated attacks of giddiness beginning 7 days after taking the last of 3 doses of 0.4 gm each, given at intervals of two days, these attacks lasted for 9 days and then diminished in intensity. (This patient also showed a rise in blood urea from 24 to 35 mgm per 100 ml.) Giddiness also required discontinuance of the treatment in two other patients receiving 10-12 mgm per kgm daily (i.e. 0.5 gm twice daily for several days). Muscular twitching occurred in a few patients and excessive sweating in others. The skin was stained yellow. One patient weighing 45 kgm who had received 1 gm daily for 7 days developed an erythematous rash over the body and face, thus disappeared after a few days. Apart from the case of the one patient mentioned above, there was no change detected in kidney function, in hepatic function, or in the blood. In three cases, temporary changes were observed in the heart. Three of the patients treated also suffered from *S mansoni* dysentery, two were not cured, one (apparently) was sterilized temporarily but relapsed. In cases which responded, the excreta became negative 7-10 days after the end of treatment. Apparently miracil does not have a direct action on the eggs. Three additional patients were each given 1 gm daily for 7 days, and viable ova had completely disappeared within three weeks of the end of treatment.

It is concluded that the effective dose of miracil is not less than 18-20 mgm per kgm daily for 7-8 days, and that the blood concentration must reach 0.3 mgm per 100 ml

F Hawking

HAWKING F & ROSS W F Miracil D Its Toxicology Absorption, and Excretion in Animals and Human Volunteers. *Brit. J Pharmacol. & Chemother* 1948 June v 3 No. 2, 167-73 "figs."

Miracil D synthesized in Germany is the hydrochloride of 1-methyl-4- $\beta$ -diethylaminoethylaminothioxanthone



and showed promise against infections of *Schistosoma mansoni* in mice. The present authors have studied its effects and blood levels in mice, rabbits, monkeys and human volunteers. It has an irritant action on tissues giving rise to inflammation and necrosis at the site of injection and it causes slight spasm of intestinal muscle. It is more toxic when given intravenously and may produce venous thrombosis. Oral dosage proved most satisfactory. Details of dosage are recorded. In man 0.2 gm. repeated daily was tolerated. The method of LATNER *et al.* [this *Bullet* 1948, v 45, 867] was used for estimation. When the drug was given orally in a single dose absorption was rapid and the blood level attained in some animal experiments was constant for at least 24 hours, but was not always proportional to dosage. In man the concentration in leucocytes, plasma and red cells was in the order given. The drug was present in most tissues of the body. About 7 per cent. of an ingested dose was excreted in urine and less in faeces, and the drug disappeared from these excretions in 1 to 3 days after treatment. About 90 per cent. appeared to be degraded in the body with consequent little tendency for accumulation. In animals, overdose caused pathological changes in liver and kidney while in man nausea, prostration, insomnia and yellow discoloration of skin and sclerotics were encountered. J. D. Fulton

MARILL, F. G. La bilharziose vésicale en Algérie. Programme de prophylaxie [Urinary Schistosomiasis in Algeria: the Programme for Prevention.] *Cahiers Méd. U. s. m. F. algérie* Algiers 1947 Nov v 2, No. 14 677-91

In January 1947 a focus of infection with *Schistosoma haematol* m was found at Fondouk, and known foci exist at Djanet and Saint-Aimé-de-la-Djiboutia. The Fondouk focus is only 84 kilometres from Algiers.

Schistosomiasis may be introduced into Algeria from Southern Tunisia, Morocco and especially from south of the Great Atlas mountains, but there are now there several established foci in the country and in many other places *Bulinus* snails are found. The author mentions *Bulinus truncatus* (and *B. contortus*, *B. dybowskii* and *B. nana* which others regard as synonyms of the first), *B. pumilus*, *B. tricus*, *B. trondeli* and *B. maris*. He makes the point that if snail hosts are present in collections of water prolonged contact with carriers of the infection is necessary before a focus is started. Irrigation canals are suitable for snails and for human contact and the disease is largely associated with irrigation systems. The smaller canals are most frequently infected. In Saint-Aimé the number of snails has diminished as a result of deliberate periodic drying of the canals but this is probably not enough to account entirely for the diminution that has taken place. Other influences have probably affected this compared to the new colonies of snails, but they are not understood. Cemented canals in that area contain only *Melanopsis* which contain chiefly *B. nana* and only rarely the grove.

# *Helminthiasis*

Vol 45, No 9]

The author discusses control The number of foci of snail hosts in Algeria is so large that in practice they cannot be dealt with, but the foci connected with irrigation can be controlled, and on these all efforts should be expended. Patients should, of course, be treated, especially soldiers drafted into these areas from Morocco and elsewhere, but examination by cystoscopy has shown that 80 per cent of African soldiers may be affected, and the trouble and expense of a complete treatment programme would be so great that it is doubtful if it could be carried through. Workmen entering from Southern Morocco should be examined at the frontier, but frontier posts are very easily avoided. Nevertheless, it is possible to control these men so that they are not permitted to stay or work unless certified as free from schistosomiasis.

For control of snails it is necessary that engineers and others engaged in irrigation work should constantly bear in mind that snail elimination is an essential part of the work. In each irrigation system there should be a full-time sanitary section directed by an expert chief. Earth canals should be cemented. Canals should be dried periodically—at Saint Aimé, experience has shown that *Bulmus* snails cannot withstand 6 hours of summer sunshine in a dried cement canal, but shade along the edges prevents this lethal action. Earth canals give much more protection to the snails. Certain sections of canal, and the larger canals, can rarely be dried, but the author suggests that these larger channels might be doubled and therefore used alternately, or provided with sluice-gates at intervals so that sections may be dried in turn. Copper salts may also be used, but if a copper compound were introduced to a strength of 1 in 200,000, which is usually required for *Bulmus*, there would be needed, for the Saint-Aimé system alone, some 650 tons each year. If, however, copper salts are reserved for parts of the system permanently under water—siphon pits, small reaches, pools, etc.—which form the reservoirs of snails, they may be most useful.

Such measures are useful for the control of schistosomiasis, but they are also of considerable value for the control of malaria in that they entail careful watch on permanent collections of water. Each irrigation system, however, presents its own peculiar problems.

Charles Wilcocks

KOURÍ, P. Diagnostico, epidemiologia y profilaxis de la Fascioliasis hepatica humana en Cuba. *Síndrome eosinofílico febril* [Diagnosis, Epidemiology and Prophylaxis of Human Fascioliasis in Cuba] Kuba Habana 1948, Mar, v 4, No 3, 63-7 [48 refs]

Clinical diagnosis of infestation by *Fasciola hepatica* is not easy, the main symptoms are those of cholangitis, cholecystitis and hepatic colic which may, of course, be due to several other causes. Finding of the ova in the faeces is conclusive but not infrequently the diagnosis has been made when an operator is in progress, or even at autopsy. Eosinophilia, especially if of an epidemic character and accompanied by prolonged fever and leucocytosis, perhaps with shivering and a painful enlarged liver, is a helpful indication. Apart from direct faecal examination and the persistent eosinophilia, complement fixation, precipitin- and intradermo-reactions with extracts of the trematode may be tried, but these are not yet established procedures. The therapeutic test—clearing up of symptoms on administration of emetine is not of much value, an amoebic hepatitis would be cured by the same treatment. From the epidemiological point of view, the infestation of cattle is all important. One record of 549 cattle slaughtered at the municipal abattoir of Pinar del Rio gave 61.9 per cent with *F. hepatica* in the bile-ducts. Generally speaking [no figures are given] human fascioliasis is more common in the white than in the negro, more in the middle and upper classes of society

O'NEAL, RUTH & MACARTH, T. B. *Trichostrongylus* Infection of Human Beings: Report of Three Cases. *Proc. Staff Meetings Mayo Clinic* 1947 May 14 v. 22, No. 10 193-7 2 figs.

*Trichostrongylus* infections were diagnosed by finding eggs in the stools of two boys aged 5 and 7 respectively and a man of 78 years. The two boys had lived in the Belgian Congo and French Equatorial Africa from an early age and the adult had spent 13 years in Korea.

A good series of photomicrographs illustrates the progressive development of the eggs up to the embryonated stage. The eggs measured from 76 to 86  $\mu$  in length by 44 to 47  $\mu$  in width. J. J. C. Buckley

BYRAL, V. L. *ber die Wirkung des Benzolens auf die Darmparasiten und seine Folgen.* [The Effect of Pure Benzene on Intestinal Parasites.] *Schweiz. med. Woch.* 1948 June 12, v. 78, No. 23, 571-2.

Petroleum and benzene have been used for some years in Asia for the treatment of intestinal parasites, particularly by veterinarians for treating ascarids and strongyloidiasis in horses and the author has undertaken a study to determine the uses of benzene and whether its exhibition has any disadvantages and sequelae. The benzene on the market is not pure—it is mixed with 15 per cent methyl alcohol and lead and is therefore dangerous. By distillation a pure product has been obtained. Starting with 0.3-0.8 cc. for each year of life as a minimal dose he obtained no result so he gradually increased it to 20 cc. for a child of 5 years, 30 cc. for those between 6 and 14 years and 60 cc. for an adult. Burning sensation in the stomach and anus was observed by giving the drug emulsified in syrup and gum arabic with a little oil of pepper mint. It is given in the morning, before food is taken, and is followed by a purge of sodium sulphate. After 2-3 hours light food may be given such as soup, milk, pap, potato, consomme, fruit juice etc.

In this way the author has treated 57 cases of ascariasis, 48 of trichuriasis, 45 of oxyuriasis, 5 of ankylostomiasis and 14 of mixed infestations. Relapses have been observed in 7, 4, 8, 1 and 0 respectively. Symptoms of intoxication are few and slight, in fact almost negligible—they included a tendency to drowsiness, some giddiness and nausea, rarely vomiting, and burn sensations in the stomach and at the anus. In animal experiments as much as 8 gm. per kilo was given to dogs without producing any toxic symptoms.

H. Harold Scott

LACE, C. Bancroftian Filariasis. Biological Mechanisms that underlie its Periodicity and other of its Clinical Manifestations. *Trans. Roy. Soc. Trop. Med. & Hyg.* 1948 May 41 v. 8 717-84 7 charts & 58 figs. on 20 pls. (Numerous refs.)

Opinions as to the causes of microfilarial periodicity have so far been mainly based on theory—some authors, like FORTSON and HODGKIN (this Bulletin v. 1936 v. 38 149) regarding of any satisfactory plan to discuss the matter as of little importance as it is a fact but by others it is regarded as embodying a vital principle. It is claimed by LACE that speculation on this subject has so far been based insufficiently on histological studies but these have now been made possible as a result of some 25 filarial sections impregnated to him by the late Professor F. W. O. CURRIE. Regarding the histological aspect of the mechanism of periodicity MEYERS (1888) held that the post-embryonic female filariae were continuous and that the embryos remained in the lymphatic system for 12 to 24 hours when they entered the bloodstream they were destroyed during the daylight hours. MEYERS (1889) on the other hand

suggested that reproduction was continuous, but that the embryos were filtered out in the lungs during the daytime. He thought that the object of Nature in making this creature so prolific was, to provide as many chances as possible for the continuance of the species, and so he found it difficult to understand why animalcules which can live many days *outside* the body of their host should die after so short a life *within* it.

From a reconsideration of Manson's data on the numbers of microfilariae present at the same hours in the blood and in lymph measured by chyle deposited in urine, it appeared that a periodicity in the lymphatics was emphatically present, but according to Lane, this differed from that in the blood by observing a morning peak. At first it appeared to Manson that filarial disease, such as lymph scrotum, could be brought about by the activities of one parent worm, but Myers recorded that the human host could harbour many at the same time. From O'Connor's serial sections it has been confirmed that 80 worms (either killed by the fixative or already defunct) could be found in a set of inguinal lymph glands in one case, and over 30 in a second. Therefore periodic parturition by one single worm cannot be held to account for the cyclical appearance of embryos in the peripheral blood.

Since the acceptance of ASCHOFF's conception of the function of the reticulo-endothelial system as a destructive and defensive mechanism, and by taking thus into account, the long life of the microfilaria outside the body can no longer be taken as evidence that an equally long one can be expected within the human host. Nor could Manson visualize that, though a great mortality of the microfilariae would ill serve the parasite, it would ultimately benefit the human host. Thirdly Manson did not appreciate the fact that the lymph flow does not cease at death, but that at *post mortem* the flow of lymph may be prolonged or even increased, so that after death it may have borne microfilariae into unexpected situations. Therefore his findings that microfilariae harbour by day in the lungs and the larger systemic arteries and thereby produce periodicity by disappearance from the skin blood can no longer be accepted as correct [but see reviewer's comment, below]. It was in 1929 that Lane, on the arguments stated above, formulated his cyclical parturition theory. He found himself incapable of conceiving a possible daytime withdrawal of microfilariae from the cutaneous to the deep capillaries. If this was the case then there must be either a periodic contraction of these capillaries, or a periodic posturing of microfilariae within them during the day. In the case of the nocturnal *W. bancrofti* these forces would have to come into action by day only, by night in the case of *L. loa*, and at no time in the cases of *A. perstans* and the non-periodic Pacific variety of *W. bancrofti*. What would happen in a double infection of two species of periodic microfilariae under these conditions beggars imagination.

As is well known, Lane's theory postulates that periodicity must be due to simultaneous microfilarial parturition once in 24 hours by the females, and the periodic destruction of these newly-born embryos within the organs each and every day. At this point the story digresses to discuss the pertinent question of the mechanism underlying the regular rhythms of inflammatory attacks in Bancroftian filariasis. A possible route by which microfilariae may migrate from the vicinity of the parent worm in the lumen of the lymphatic through its walls to neighbouring small blood vessels, on their way to the general circulation, has now been demonstrated, though it is not claimed as the normal method. It has been believed that death and destruction of microfilariae in process of transit cause attacks of acute inflammation. Thus O'Connor thought that in sections of a lympho-varicocele he had obtained visual evidence of this transit. The larval sheaths (as in other nematode larvae) are separated, but enclosing cuticles which are cast at the last ecdysis, and therefore should be

discarded in this transit. During the development of the larva in the intermediate host it escapes from the sheath by fixing the anterior end of the sheath against an obstacle and by boring through it towards that obstacle. Normally this is the midgut of the mosquito but this thigmotactic urge, it is claimed, is present during its sojourn in the human definitive host and is revealed by the actual presence of discarded sheaths in the viscera (illustrated by two microphotographs in the text, the interpretation of which is open to some doubt). On the other hand, penetration of tissue without loss of sheath is possible as has been demonstrated by HAWSON in *Leishmanoides pullerossi* of the cotton rat.

Mammalian striped muscle is exceptionally rich in lymphatics and is a possible route (lymphatic escalator) for microfilariae from the pleural lymph sac along the rich plexus of the diaphragm towards the great veins. On the other hand, active penetration of *W. bancrofti* from lymph to blood must be a rare event because otherwise sheathless microfilariae would commonly be found in blood preparations.

No evidence however has been forthcoming that acute inflammatory attacks are connected with massive birth of microfilariae to their subsequent burrowing through the tissues or to their death in these situations. On the other hand Lane believes that a superadded bacterial infection is much more likely to be responsible for acute lymphangitis. For the species to survive it is obvious that the numbers of circulating microfilariae must be kept up by new births in order to make good the wastage. Should these births take place periodically at the time of, and be the cause of, fever and inflammation, then a number must reach the bloodstream, and therefore an increase in the number of circulating microfilariae should be expected, but just the reverse is the case.

Some space is devoted to the fifth theory (HALL, this Bulletin 1909, Vol. 33). This assumes a more or less continuous parturition, and the course of periodicity is ascribed to special siting of parturient female worms, to gravity, and to periodic flow of chyle but there is no evidence that any of these factors is operative.

YOKOGAWA's theory (Trans. Roy Soc. Trop. Med. & Hyg. 1909 v. 33 363) is even more unlikely. He suggested that the periodicity of microfilariae is chiefly controlled by the diurnal and nocturnal alterations of the physiological functions of the reticulo-endothelium. There is no proof whatsoever that such an intrinsic variation of activity of this system is operative.

Evidence is now offered that in periodic Bancroftian infection two opposing forces operate: (1) synchronized peristaltic parturition and (2) local macrophage activity in the lymphatics and lungs, which brings about complete or partial destruction of the microfilariae.

The points to be established should be that: (1) Periodicity was established at the time the specimens were procured. (2) The worms studied had been killed at the time the tissue was fixed. (3) All the female filariae were in the same stage of parturition. (4) The uterine state corresponded to a synchronized periodic emptying. (5) The phases of microfilarial blood take were in accord with the differences in the uterine content.

In order to give effect to his findings a detailed description is given by the author of the tubular genital tract of the female *W. bancrofti* special attention being directed to the vaginal pouch (COWDRIE) a study has been made of the worm in tissues when killed by fixative.

From the detailed consideration of the changes observed in the uterine contents, the author concludes that there is a stage in which the uterine horns and the anterior branches are filled with outstretched embryos lying for the most part parallel to the uterine axis. When uterine peristalsis sets in, these embryonic forms are expelled and their place is taken by upstarting young developing from eggs. The appearances are those of a process of expulsive

emptying parturition, followed by uterine refilling from the ovaries. Pre-microfilarial young are commonly found free in the tissues of the host. This observation was originally used by Manson as the basis of his theory of lymph stasis. But in O'Connor's material these forms were commonly found in lymphatic glands, together with normal microfilariae. The evidence is that many young are born while still coiled within the egg membrane and that they may subsequently rupture and escape from it.

When the microfilariae are found in numbers in by-passing lymph capillaries or in lymph glands, their situation is such as would be caused by a process of expulsive emptying parturition. The main factor in ascertaining from microscopic sections the level to which parturition may empty the uterus is the observation that at any level all the contained microfilariae are at much the same stage of development, but do these synchronized emptying parturitions cause the rise of the microfilarial blood tide? This is answered by the following facts—(1) The tides were present when the specimen was obtained, (2) blood obtained by skin-prick was found enough to establish periodicity, and (3) the parturition of the worm took place at an hour reasonably related to that at which the microfilarial blood tide rose. In lymph glands removed between 13 45 and 14 28 hours [1 45 and 2 28 p.m.], O'Connor found that the uterine stems of the inhabiting filariae were either empty or contained eggs only. In necropsy material, that obtained from persons dying about midnight was particularly helpful. Out of six autopsies in which these conditions were recorded, satisfactory findings were obtained in two only. Nevertheless the findings are stated to be such as would occur if synchronized parturitions expelled a swarm of microfilariae into the lymphstream at such a time as would cast them into the blood during the normal period of the microfilarial tide.

Whatever may be the mechanism underlying periodicity, some stimulus must surely attract the microfilariae into the skin blood at night. This synchronizing stimulus remains unknown. Possibly it may be through the male bringing about coitus and impregnation at a certain hour, or through the female by exciting parturition at a certain hour and thus leaving the uterus empty. The stimulus comes into being once in 24 hours, but produces a response in parasites only when they are ready for it. In the periodic Bancroftian filariasis all female adults are ready for it every night, but here again difficulty arises when stipulating what happens for the non-periodic form, for *A. perstans* and for *L. loa*. The author discusses at length the larvicidal mechanisms which interfere with the rise of the microfilarial tide. It is well known that microfilariae, though born, may not reach the blood. Reasons are given against the belief that embolisms of still-coiled embryos can effectively dam the lymph current through a lymphatic gland, but probably the microfilariae are held back, imprisoned and destroyed by active proliferation of the cells of the macrophage system. By these means the lymph current is slowed down and the microfilariae held where these cells are most numerous. The end result of these larvicidal mechanisms is to produce ever-increasing lymph stasis and such clinical results as hydrocele and elephantiasis. These effects arise from two interacting factors—excessive extracellular lymph protein, and fibroblastic activity. The fibrous formation that they induce round the lymphatic tract contracts and interferes with the further free flow of lymph through it.

There is an analogy between the effects of raised blood pressure and lymph pressure. Vessels become dilated and where they have muscular walls these are thinned or thickened. The earliest evidence traced for this dilatation goes back to Manson's observation of skin vesicles that, when ruptured or pricked, discharged microfilariae. The accompaniment of elephantiasis is presumably due to an increase of extracellular protein in the lymph, brought about by

discarded in this transit. During the development of the larva in the later molted host it escapes from the sheath by fixing the anterior end of the sheath against an obstacle and by boring through it towards that obstacle. Normally this is the mudgut of the mosquito but thus thigmotactic urge it is claimed, is present during its sojourn in the human definite host, and is revealed by the actual presence of discarded sheaths in the viscera (illustrated by two microphotographs in the text the interpretation of which is open to some doubt). On the other hand, penetration of tissue without loss of sheath is possible as has been demonstrated by Huxford in *Leishmaniasis patersoni* of the cotton rat.

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PEEL, E & CHARDOME, M. Note complémentaire sur des filarides de chimpanzés *Pan paniscus* et *Pan satyrus* au Congo Belge [An Additional Note on the Filarial Worms of the Chimpanzees, *Pan paniscus* and *Pan satyrus*] *Ann Soc Belge de Méd Trop* 1947, June 30, v 27, No 2, 241-50, 8 pls

The previous discovery by PEEL & CHARDOME [this *Bulletin*, 1947, v 44, 339] of the adult female *Dipetalonema streptocerca* in chimpanzees, is now amplified by a description of the male adult. In addition they have found and identified the adult forms of *Mf rodhaini* Peel & Chardome, 1946, and assign them also to the genus *Dipetalonema*.

Three male *D. streptocerca* were collected from the subcutaneous connective tissue of two chimpanzees, *Pan troglodytes schweinfurthi*. They measured 17.5 to 18.1 mm long with a maximum diameter of 46.66 $\mu$ . There are three pairs of pre-anal and two pairs of post-anal papillae and a sixth pair 26.66 $\mu$  from the caudal extremity, which is described as terminating in two cuticular prolongations. [This description is incompatible with the figures illustrating the ventral and lateral views of the male tail. The two figures are also incompatible with each other.] The unequal spicules average 338.8 $\mu$  and 117.4 $\mu$  long respectively, and there is a small gubernaculum.

Three female and one male *D. rodhaini* were collected from the subcutaneous connective tissue of *Pan troglodytes schweinfurthi*. The male is 19.9 mm long with a maximum width of 53.32 $\mu$ . There are two pairs of pre-anal and two pairs of post-anal papillae, and a single pair situated 6.66 $\mu$  distant from the latter. The diameter of the single pair of papillae is twice that of the anal papillae. [This makes a total of five pairs of papillae but in the drawing there appears to be a sixth pair between these and the tip of the tail.] The unequal spicules are respectively 366.63 $\mu$  and 143.31 $\mu$  long. The average length of the female worms is 25.216 mm and the maximum width 83.3 to 86.6 $\mu$ . The genital opening averages 502.15 $\mu$  from the anterior extremity.

J J C Buckley

VARGAS, L. Los simulidos en la transmisión de la Oncocerciasis Americana [Simulium and the Transmission of American Onchocerciasis] *Medicina Mexico* 1948 May 10 v 28, No 555 177-90 [66 refs]

A general account with bibliography

GAYTON, J. L. BELLIS, M. & McCLENNAN, W. H. A Survey of Pinworm Infection in an Elementary School *Canadian J Pub Health* 1948 May, v 39, No 5 200-202

The public health nurse in an area in South Vancouver received repeated reports from mothers concerning minor symptoms in their children attributed to pinworms (*Enterobius vermicularis*). The authors therefore examined 145 of the 160 children in the local village elementary school. Examination was made by means of the Graham swab (three inches of "Scotch tape" held sticky side outwards over the end of an applicator). The swab was then dipped in dilute iodine solution and applied to a microscopic slide for examination.

Of a total of 5144 slides 982 (or 19.1 per cent) were positive. Where more than 100 slides were examined in a village the incidence varied from 13 to 25.8 per cent.

The blood of children under 5 years of age was not examined. In the succeeding quinquennial periods the incidence of positive slides rose regularly from 5.2 per cent. (age 5-9) to 43 per cent. (age 50-54) and then irregularly up to 50 per cent. (age 75-100). The average number of worms per slide showed a steady rise up to the 50-54 age group (30.7) but after this tended to fall and was 11.1 in the highest age group.

The rate for microfilariae among men was almost double that of women in all age groups above the age of 20 years.

Elephantiasis was not observed in any person less than 30 years of age. Of 1,573 persons over the age of 30 years from whom blood slides were taken, 61 (or 4.2 per cent.) showed elephantiasis. If hidden parts such as the scrotum had been examined the rate would have been considerably higher. Of these 51 (5.8 per cent) were men and 13 (21 per cent.) women. The incidence was correlated with the age.

Of the 66 persons with elephantiasis 32 (48.5 per cent.) showed microfilariae in the peripheral blood. The microfilaria rate for a total of 1,573 persons of 30 years or over was only 36.8 per cent. The author concluded that "Samoans with elephantiasis had a considerably higher rate of microfilaraemia than did Samoans without elephantiasis, when comparable age and sex groups were considered."

[The author discusses the results and draws his conclusions as if his figures had been obtained on a strictly quantitative basis, whereas the technique adopted would only allow of qualitative results—e.g. the amount of blood taken was not measured but it is stated that it approximated 20 cubic millimetres.]

L. E. Nafier

WHARTON D. R., A. CERRAJO, C. & MOYER A. W. Skin Reactions in Sensitized, Infected and Normal Rabbits with Filarial and other Nematode Antigens. *J. Infect. Dis.* 1947 Nov-Dec, 58: No. 3, 54-60. 15 refs.]

Rabbits were sensitized with saline extract of larvae and the filarial worms *Dirofilaria immitis* and *Leishmanoides car* and by infection with *Trichinella spiralis*. When these rabbits were tested intracutaneously the different antigens reacted specifically and there was no significant reaction with filaria antigen in the filaria sensitized rabbits.

"However in the trichinosis rabbits all the antigens reacted strongly although *Trichinella* antigen was negative in the heterologously sensitized rabbits.

"There was evidence of reaction by filaria in a few of the two filaria sensitized animals. This may have been due to specific sensitization by obscure ascared infections.

"It is concluded that in skin tests for filariasis cross reactions with intestinal helminths such as filariae do not ordinarily occur.

SCOTT J. A. Studies on the Transmission of the Filarial Worms of the Cotton Rat. *Amer. J. Trop. Med.* 1948 May, 24: No. 3, 461-5.

"A method is described for infecting groups of cotton rats with a relatively constant number of the filarial worms *Leishmanoides* or all of which are of the same age. The infections were produced by placing the animals in metal tanks containing numbers of mites whose percentage of infection had been

# Helminthiasis

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A general account with bibliography

GAYTON, J L BELLIS M & McCLENNAN W H A Survey of Pinworm Infection in an Elementary School. *Canadian J Pub Health* 1948, May v 39 No 5 200-202

The public health nurse in an area in South Vancouver received repeated reports from mothers concerning minor symptoms in their children attributed to pinworms (*Enterobius vermicularis*) The authors therefore examined 145 of the 160 children in the local village elementary school Examination was made by means of the Graham swab (three inches of Scotch tape," held sticky side outwards over the end of an applicator) The swab was then dipped in dilute iodine solution and applied to a microscopic slide for examination

The results as shown in four tables. Altogether 38 children were found positive and 21 others were "known positive" in that pinworms had been seen by the parents. Twelve in the latter group were not examined for it. Thus 59 (57.8 per cent) of 157 children were positive.

There were 116 families represented in the school and 48 of them were shown to have pinworm infection in the family. The median length of residence of these families in the district was only two years. Pinworm cases were found in every type of family. Infection was highest in the younger children: there were 50 per cent. positives in school grades II and III and only 7 per cent. in grades V and VI. The geographical distribution of cases was comparable to that of the general school population.

After the examination, the public health nurse visited each of the 48 "positive" families. Symptoms attributed by the parents to pinworm varied from convulsions and coma in one small child to abdominal cramps, nausea, restlessness, poor sleep, anorexia and underweight. In an adult, simple pruritus ani was the only symptom.

Many of the children had been treated previously, so that either the treatment generally used was ineffective or reinfection occurred. The treatment recommended was gentian violet enteric-coated tablets thrice daily in standard dosage in two 8-day series one week apart. The whole family was usually treated, with few complaints of nausea or diarrhoea. Quarsa earwas and ammoniated mercury ointment were also used. Linens and bedding were boiled.

The authors observe that reports in recent journals would suggest that their findings were not unusual and that the percentage of 57.8 found by them would probably indicate a true incidence of some 50 per cent. positives. Enteric infection as a public health problem requires further study.

H. J. O'D. Burke-Gaffney

## HAEMATOLOGY

STEPHEN J. D. Haemoglobin and Plasma-Protein Levels in West Africa.  
*Trans. Roy. Soc. Trop. Med. & Hyg.* 1948, May. 41, No. 6, 829-31.

Because of the prevalence of dietary deficiencies and anaemias in West Africa, the author in the Gold Coast compared the haemoglobin and plasma-protein levels of troops of the Royal West African Frontier Force with those of the civilian population to determine whether army life had any effect in increasing haemoglobin values.

Seven groups of 50 persons each were studied namely (1) African recruit with 6 weeks' service; (2) African soldiers with 6 to 8 months' service; (3) African soldiers with 2 or more years' service who had been in India, had been on a European-scale ration and in many cases had taken suppressive mepacrine; (4) African male civilians from coastal villages; (5) African children from coastal villages; (6) pregnant African women; (7) European soldier stationed in Sierra Leone for 3 to 18 months.

The tests were made on 5 cc. quantities of salinated blood (10 mgm. ammonium oxalate mixed with 4 mgm. of potassium valate). The specific gravity of the whole blood and of the plasma was determined by the copper sulphate method of PHILLIPS *et al.* (*Copper Sulphate Method for the Specific Gravity of Blood and Plasma* 1943, New York: Josiah Macy Junior Foundation) and the haemoglobin and plasma-protein levels were read from a single line chart.

The results are shown in two tables. The African haemoglobin levels generally were lower than the European, but a high level was found in the soldiers of group (3), as might be expected, in view of their diet and freedom from malaria in most cases. Their mean haemoglobin in gm./100 cc was 15.1 compared with 15.4 for group (7), the European soldiers, and 14.2 for the soldiers in group (2) and the male villagers in group (4). The levels in pregnant women and in children were 11.4 and 12.2 respectively, the frequency of macrocytic anaemia in the pregnant women and of malaria in the children would lead one to expect such figures.

There were no significant variations between the plasma-protein levels in the Africans and in the Europeans.

Since the highest African haemoglobin level was found in the troops who had had a European-scale ration and, in many cases, suppressive mepacrine, the author concludes that "it is thus possible to effect a rise in the African haemoglobin level so that it equals that of the European."

H. J. O'D. Burke-Gaffney

DEWHURST, K. E. *The Normal Lobular Neutrophil Picture in the East African*  
*J Trop Med & Hyg* 1948, June, v 51, No 6, 128-30

The author discusses the principles and significance of the Arneth count and the polynuclear count of Cooke and Ponder and also discusses the findings of a number of workers in the Tropics who found a "shift to the left," both in health and disease [this *Bulletin*, 1937, v 34, 259, 1942, v 39, 54]. He notes that KENNEDY and MACKAY [*loc cit*, 1937] attributed a normal "shift" to climatic conditions, as in the case of Europeans the Cooke-Ponder weighted mean became normal on their return to Europe. In health a lower weighted mean than 2.75 or a higher Arneth index than 58.5 indicates a "shift to the left."

The present author examined blood films from 500 healthy East Africans. 330 were examined in Kenya and 170 in South-East Asia Command. Four tribes were included, but tribal variations in results were negligible.

The Arneth index and the weighted mean were found respectively to be 73 and 2.4, indicating a "left shift" in these Africans compared with the European standards quoted above. In the case of the Africans, the author took the normal limit of the Arneth index to be 65, which is the extreme limit in the European range (given as 51 to 65), and on this basis estimated that 82 per cent of the blood films examined showed a "left shift," which was significant (above 70) in 65 per cent. The figures are shown in tables in the text.

It is suggested that, in addition to the effect of drugs or toxic absorption, an increase of immature neutrophils in the peripheral blood may be stimulated by climatic conditions. The author considers that this is due not to exposure to ultra-violet light, but to the thermal effect of a tropical climate. It is noted that such a shift was found in places with a high humidity (Calcutta) where the effect of ultra-violet rays is diminished owing to their high absorption.

The results show in general that most of the Africans examined showed a "shift to the left" owing to a marked increase of cells of Class II.

[The present reviewer studied the Cooke-Ponder polynuclear in health and disease in East Africans in 1931 (this *Bulletin*, 1931, v 28, 837). He also found some "shift to the left" in a control group which were taken to be healthy Africans, but to find the "normal" African, the most careful clinical examination was required in order to exclude any possible factor which might influence the blood counts. In the present author's case, the men examined would of course constitute a much more reliable "healthy" group, since they were controlled troops under constant medical care. The author's suggestion

that the "left shift" might be due to the thermal effect of a tropical climate is interesting, but would require more concrete evidence in its support.)

H J O D Burke-Gaffney

WILKINSON J F Falls AcM. Brit. M. J. 1948, Apr 4 & May 1 771-4  
822 7 2 figs. [101 refs.]

## VENOMS AND ANTIVENENES

TRETHEWIE E. R. & DAY A. J. New Therapy of Ophidiasts. 4 *Weeks J. Exper Biol & Med Sci* 1948, Mar v 28, Pt. 2, 153-61 5 figs. [17 refs.]

It was found that neo-antergan injected subcutaneously into mice after the previous injection of *Pseustes porphyreus* venom subcutaneously did not reduce mortality.

"Neo-antergan when injected with heparin into mice reduced the mortality following the injection of venom from 50 to 5 p.c.

"A rise of pulmonary arterial pressure was detected in the cat following the injection of this venom but this rise was not affected by previous treatment with neo-antergan.

"The significance of these findings and the rôle of this form of treatment has been discussed."

SERGEY E. L. Sur le venin des scorpions *Prionurus australis* L. et *Prionurus amarus* C. Koch. On the Venoms of *Prionurus australis* and *Prionurus amarus*. [Arch. Inst. Pasteur d'Algérie 1948 Mar v 28, No. 1 21-4 1 fig]

The author has found by repeated experiments, that the venom of *P. australis* is more potent than that of any of the other North African scorpions. The fatal dose for white mice 20 gm. weight is 1/40-1/20 telson the higher dose causing certain death in 2 hours. In previous studies, Professor Sergent has compared this with another scorpion which he called *P. lewisii* whose venom is less than one-sixth as toxic 1/3 telson being the m.l.d. for these mice. He now finds that what he has been calling *P. lewisii* is in reality *P. amarus*. He gives descriptions of both these indicating the differences. In a list he gives the lethal doses of the 7 common species of scorpions in North Africa and incidentally shows that the common belief that the black scorpions are the most dangerous is erroneous—the third, fourth and sixth in the following list are black. The m.l.d. is 1 the dried powdered telson *Prionurus striatus* 1/20th telson *P. amarus* 1/15th *P. argenteus* 1/12th *P. aeneus* 1/3rd *Buthus occidens* 1/1 *Hottentotta gentili* 3/4 1 *Scorpio maurus* 7 telsons.

H Harold Scott

VACHON M. Etudes sur les scorpions. A Study on Scorpions. [Arch. Inst. Pasteur d'Algérie 1948, Mar 28 No. 1 25-31 24 figs.]  
A comprehensive anatomical study

## ERRATUM

In the abstract of the paper by MARJA and this *Bulletin* 1943 45 340-41 the word "it" was found that the "I" was then formed by the locustian on the

blood suspensions were stabilized. It is believed that venom is the stabilizing substance" should read "it was found that blood suspensions were stabilized. It is believed that the lysocithin formed by the lecithase in the venom is the stabilizing substance."

## DERMATOLOGY AND FUNGUS DISEASES

CALERO, C. **Chromoblastomycosis in Panama. Report of a New Case and a New Clinical Form.** *Arch Dermat & Syph* 1948, Feb, v 57, No 2, 266-71, 4 figs

The author describes an unusual clinical form of chromoblastomycosis in Panama, in which the lesions were not confined to a single area of the skin. The earliest lesion appeared on the antero-external aspect of the left leg as a small nodule which slowly spread until it attained a diameter of 16 cm. It was verrucose but not markedly hypertrophic, it bled easily from slight trauma and it was surrounded by a number of satellite nodules. A second lesion developed on the back of the right middle finger. It measured 5×6 cm and was covered by white, greasy scales, the removal of which caused slight bleeding and exposed a smooth, glistening surface more eczematoid than psoriasiform in appearance. Scrapings from both lesions showed the characteristic pigmented fungal cells of the disease, and *Fonsecaea pedrosoi* var *communis* was isolated from these in culture. A third type of lesion developed later as a well-demarcated infiltration of the skin, without scaling, excoriation, vesiculation or formation of verrucae on the neck and the flexures of the extremities. The fungus was not found in this kind of lesion and it was believed to be an allergic manifestation of the disease.

J T Duncan

WEED, L. A. & PARKHILL, Edith M. **The Diagnosis of Histoplasmosis in Ulcerative Disease of the Mouth and Pharynx.** *Amer J Clin Path* 1948 Feb, v 18, No 2 130-40, 4 figs [65 refs]

In histoplasmosis, a disease of protean symptomatology, the diagnosis rests inevitably on the discovery of *Histoplasma capsulatum* in the lesion, by microscopy or by culture and therefore, accessible lesions such as the ulcerating granulomata which sometimes occur in the mouth are of particular importance for diagnosis. The authors describe lesions of this kind in four cases of generalized histoplasmosis. In one case, they took the form of ulcers measuring 1 cm in diameter with heaped-up edges, on the faucial pillars and epiglottis; in another, there were multiple small punched-out ulcers near the tip of the tongue which prevented its protrusion because of the pain they caused; in the third case, patches of hypertrophied mucous membrane containing small red nodules simulated epithelioma, but the underlying granuloma was characteristic of histoplasmosis and in the fourth, in addition to granulomatous lesions on the soft palate and neighbouring areas a large ulcer involved almost the entire floor of the mouth and a smaller ulcer was found on the epiglottis. In this last case, seven different diagnoses which did not include histoplasmosis, had been made.

In all four cases, the diagnosis of histoplasmosis was based on the isolation of *H. capsulatum* in culture from the mouth lesions, but histological confirmation was definite in one case only, uncertain in two and wanting in the fourth.

J T Duncan

The action of compounds used as chemotherapeutic agents against blood sucking ectoparasites is highly specific. Thus "pivalyl-1,3 indandione is very effective with lice and relatively inactive against mosquitoes whereas gamma BHC is much more effective with lice than with mosquitoes.

J. R. BURRIS

ANDERS, J. M. & SIMMONS, S. W. Developments in the Use of the Newer Organic Insecticides of Public Health Importance. *Amer J Pub Hlth*, 1948, May 38, No. 5, Pt. 1 813-31 [134 refs.]

A general review

See also p. 829. DETERT, R. Vinc. & G. Chemical Insect Attractants and Repellents.

## REPORTS SURVEYS AND MISCELLANEOUS PAPERS

CONGO BELGE. Fonds Reine Elisabeth pour l'Assistance Médicale aux Indigènes du Congo Belge. Rapport sur l'Activité durant les années 1939 à 1945 [BRAUWERS, P.] [Report on the Work of the "Foréami" from 1939 to 1945.] 222 pp., 4 maps (1 folding) 15 figs. on 8 pls. & 20 diagrams. 1947 Brussels 112 Rue du Commerce.

The Foréami (abbreviated form of "Fonds Reine Elisabeth pour l'Assistance Médicale aux Indigènes du Congo Belge") is unique among medical and sanitary services in tropical territories. Its purpose is to provide and to maintain for long periods of time in a limited and specially backward part of the Belgian Congo a much more intensive and more costly level of medical care than could possibly be provided for the entire colony. It acts therefore as a spearhead of sanitary progress, which, the authorities hope may gradually move on to new ground, while handing over to the less well-endowed general medical services those areas which have already been reclaimed. Its activities are expected at the same time to provide valuable lessons of ideal practice as patterns which the general medical and sanitary service of the colony may strive to emulate.

The Foréami was founded in 1931, and is run on essentially autonomous lines, though in close association with the colony's general health services. Only the interest on capital funds is spent: the nucleus of the capital having been provided by 50 million francs voted by parliament, 100 million assigned by the Minister of Colonies, and 245 000 francs donated by Queen Elisabeth. To this are added donations and subscriptions by the general public. This is covered by the Foréami has changed gradually from year to year. It began in the District of Bas-Congo but this zone reverted to the general Health Services of the colony in 1934 and activities are now confined within the Districts of Moyen Congo, Lac Leopold II and Kwango covering the needs of about 625 000 people.

Until the war a Report was published annually for 1938 and 1937 Reports see this Bulletin 1940 v. 37 366, 522 1939 v. 36 408 656. The activities of 7 years 1939-1945 are reported, with a wealth of statistical detail, in the present volume under date of July 1947.

The Report gives the impression that the Foréami method is based on a distinct bias towards what may loosely be described as medical rather than sanitary forms of relief—that is, such measures as the provision of hospitals, dispensaries, itinerant treatment teams, etc. rather than the organization of rural sanitation by way of mosquito control bush clearing, attention to water supplies, propaganda, and the like.



Each touring team is in charge of a medical man, and was intended to be responsible for the welfare of 25,000-30,000 people, though the number had later to be increased to 40,000-50,000. The aim is to examine, and treat if necessary, every one of these persons once every six months. A four-year plan of intensified effort was launched in 1939, envisaging the employment of 18 European medical men, 20 European "*agents sanitaires*" and 430 African assistants. The full complement were in action by 1939, but the war naturally interfered with progress, and by 1945 only 10 medical men and 13 "*agents sanitaires*" were in the service.

Details are given, together with photographs, of newly built hospitals, dispensaries and houses. With regard to new roads the war, far from limiting this important development, actually favoured it, because of the military value of a suitable network of road communications.

So intensive and comprehensive have the Foréami's activities been that it is not easy to summarize this work adequately in any space less than is occupied by the original report. In the section on epidemic diseases notes are given for the situation year by year for each of 14 diseases or groups of diseases, such as bacillary dysentery, amoebic dysentery, smallpox, relapsing fever, cerebrospinal fever, etc. There was no frank epidemic of any kind, and there were only 311 deaths under the heading of epidemic diseases among a total of 143,073 deaths from all causes during the 7 years of the Report. There were 1,575,653 vaccinations and revaccinations for smallpox during the period.

Under the heading of endemic diseases, sleeping sickness has long been regarded as the most serious condition, outclassing even malaria in importance. Yaws is fairly prevalent, but is not an anxiety, being easily cured. More serious, but less frequent, is leprosy. There are active foci of pulmonary tuberculosis, very fatal for the African, and venereal disease is common, especially gonorrhoea, with an increasing incidence of syphilis.

When the Foréami began operations, sleeping sickness was a veritable scourge ("*un véritable fléau*"), but it has since been reduced to no more than "*une simple menace*", as a result of systematic and repeated examination and treatment of the population. All other control methods were rapidly found ineffective, mainly through lack of cooperation by the Africans themselves. In recent years, however, direct action against *Glossina* has been taken, especially by means of fly traps of the Harris type, but these efforts have met with little success. Increasing reliance has been placed on mass chemoprophylaxis, with pentamidine or propamidine replacing suramin (Bayer 205) for this purpose. Because of its activity in the nervous stages of the infection tryparsamide remains the sovereign remedy for established cases, in spite of the increasing incidence of arsenic resistance. The most effective treatment for arsenic resistant cases is a combination of suramin and tartar emetic. Out of a total of 58 505 cases of all types treated by all methods since the start of this work, 86 per cent have been cured. A striking epidemiological finding is that "the existence of an arsenic-resistant strain generally provokes a veritable epidemic flare-up, due probably to the considerable virulence of the trypanosome and its extreme transmissibility" (page 76). [This does not accord with VAN HOOFF's views (this *Bulletin*, 1947, v 44, 1048, also quoted by PELLISSIER, this *Bulletin*, 1947, v 44, 975) on decreased transmissibility associated with arsenic-resistance.]

A considerable section of the report deals with the SADAMI (*Service Auxiliaire d'Assistance Médicale aux Indigènes*), the name given to the activities of individuals or organizations not dependent directly on the government, and which are mainly various religious missions.

Appendices deal with (1) a general survey of pathological conditions encountered in the Congo, by A. FAIN, (2) Chemoprophylaxis experiments with propamidine and suramin, by A. FAIN and DRUMEL, and (3) the "buaki

or kibengi syndrome (see this *Bulletin* 1936 v 36, 91-13) by DUMAILLON and G. GUKKAS.

In some future Report of the Foréarl it would be extremely valuable if a careful comparison could be drawn between health conditions in the Foréarl zones of activity and similar perhaps neighbouring areas which have not had such preferential treatment. It would be worth while knowing whether the extra benefits derived are fully commensurate with the extra care and costs expended.

E. M. Lewis

DEVORS P. Le Touat, étude géographique et médicale. (Geographical and Medical Description of Touat. Arch. 1<sup>st</sup> Pasteur d'Algérie. 1947 Sept. Dec. v 25 Nos. 3,4 223-74 3 figs. (2 maps) and 6 pls.

In this monograph the author gives an interesting account of the geography, history, sociology and disease prevalence of Touat where he had spent two years as a medical officer. Touat consists of a group of oases in the central Sahara extending over 231 km. from north to south. The northern end lies to the south west of Laghouat.

The population consists of Arabs and Negroes. Their mode of life, manners and customs are well described and some good photographic reproductions add to the interest of the story.

Diseases of the eye are almost universal. Trachoma and acute conjunctivitis are both widespread. Weak bacillus or Muras bacillus are responsible for the conjunctivitis. Gonococcal conjunctivitis was not seen.

Malaria is endemic but the endemicity is of low intensity. From time to time exceptional circumstances have caused epidemic malaria. Thus in 1945 the opening of a *foggara*, an underground water channel, a kilometre from Adrar the capital, resulted in the formation of a marsh which provided good facilities for mosquito breeding. An epidemic of malaria followed which lasted from June to October. The spleen rates everywhere at very low. Of 77 patients blood smear examined, *P. falciparum* was found in 44, *P. vivax* in 20, *P. malariae* in 12, and a mixed infection in one. The only three mosquitoes that have been identified in Touat are *A. gambiae*, *A. sergenti* and *Theobaldia longirostris*.

Loose borne relapsing fever had never been seen in Touat till 1945. In 1945 there was a large outbreak. The author saw and treated 718 cases. Arabs and Negroes were alike affected. The case mortality rate was highest among the Negroes who are less well fed. A case was seen in infants under two years of age. Untreated cases often succumbed. Jaundice was a common symptom.

In 1941 and the two following years there were outbreaks of typhoid fever. Neither typhoid fever nor Malta fever occur. Only two cases of cerebrospinal fever have ever been diagnosed. Sporadic cases of diphtheria are seen from time to time. Tuberculosis is not very widespread. Smallpox once very prevalent is now rare thanks to vaccination. Epidemics of chickenpox have occurred. A serious outbreak of measles occurred in 1945. One of 74 observed cases terminated fatally. Scarlet fever has never been seen.

Veneral diseases are very widespread. Syphilis, gonorrhoea and soft chancre are all common.

Organic diseases of the heart are rarely observed. Acute rheumatism was not seen. Bronchitis is a common malady. Dysenteric syndromes are prevalent in May, June and October when flies are most prevalent. Clinically the cases resemble bacillary infections. Amoebic infections appear to be rare.

Famine oedema was common in 1944-45 and followed a series of deficient harvests. Some 70 per cent of the population in Larbaa Thaur.

There are no poisonous snakes. Scorpions are frequent but their sting very rarely causes death.

Norman H. Dale

UNITED NATIONS DEPARTMENT OF SOCIAL AFFAIRS POPULATION DIVISION  
Lake Success, New York **The Population of Western Samoa** *Reports on  
the Population of Trust Territories No 1* 1948, Jan 17, 61 mimeographed  
pp, 7 figs [Refs in footnotes]

In a prefatory note it is explained that " This is the first of a series of reports on the population of Trust Territories, being prepared by the Population Division in the United Nations Department of Social Affairs. The purpose of the reports is to summarize existing knowledge regarding characteristics of the population, trends of population growth, and the relation of population to economic resources in each of the territories."

The particular interest of the islands which form Western Samoa lies in the fact that the population, of about seventy thousand, is one of the most rapidly growing populations in the world. An attempt is here made to gather together all known statistics relating to it and to discuss the factors which may have contributed to this rapid increase.

The writers have, the reviewer believes, been successful in collecting all the early estimates of population starting with that which has been attributed to La Perouse (1787). These early estimates were made at irregular intervals over a period which ended in 1886, that is to say for almost exactly a century. The evidence seems to suggest that in that period the population occasionally rose above forty thousand or fell below thirty thousand, but that there was no general trend over the whole period. It seems clear that such diseases as influenza and whooping cough, which were probably introduced to a non-immune population by European shipping, produced serious epidemics and sudden reductions in the population. The report refers also to wars between different sections of the population. It is felt that hardly enough weight is given to the fact that in the nineteenth century wars had become much more deadly because the Samoans possessed weapons made of iron, and also firearms. There is little evidence that famine reduced the numbers of people.

The second period may be said to have started with German occupation of the islands in 1900. From then until 1914 a census was made on several occasions, and in 1905 regulations were brought in for the registration of births and deaths. Throughout the period of German occupancy and, indeed, up to 1920, one may say that the population appears to have increased rapidly but to have been reduced occasionally by major epidemics. Much the most serious of these is described in the following words — During the last three months of 1918 influenza struck with such violence that it not only wiped out all the gain of the preceding seven years but reduced the population to a level below that of 1911. The number of deaths reported in 1918 was over 8,400 or 7,000 more than the number of registered births. The loss amounted to nearly one-fifth of the whole population. This ranks as one of the most disastrous epidemics recorded anywhere in the world during the present century, so far as the proportion of deaths to the population is concerned. As a result, when the next census was taken in April 1921, it showed practically the same population as in 1906.

The authors call attention to the fact that throughout this second period (1900-1920) the population manifested a succession of sporadic increases interrupted by precipitous declines. This as they say, is characteristic of a rather primitive population with a high birth rate subjected to periodic catastrophes.

The third period dates from 1920 when the League of Nations granted a Mandate to New Zealand. Since that date there has been no major epidemic and the general health of the population has been steadily improved. In each year the registered births have exceeded the deaths and the population has

nearly doubled in less than a quarter of a century: the average increase being 2.5 per cent per annum. This average rate of increase is greater than that recorded for any other tropical area—for instance the Philippine Islands, in which the rate of increase is well known to be very great, has had an average of 2.3 per cent. over a comparable period.

Other parts of this interesting document discuss the proportion of leprosy and people of mixed blood in the Samoan population, also birth and death rates, and immigration and emigration. One receives an impression that the text has been written at least in part by men familiar with the problems on the spot and fully aware of the difficulty of accumulating vital statistics through village headmen literate only in a Polynesian tongue. It is noted also that the report gives due and expert emphasis to social conditions—for instance the section on the density and distribution of the people is closely related to that on the economic development of the country.

The final chapter discusses the probable future of the Samoan population, which will have reached about 150,000 by 1975 if the present rate of increase continues—that would give the very high density of 250 per square mile of cultivated land. Clearly then there is an urgent need for the study of soil, economics and agriculture and for the improvement of agricultural methods so as to ensure that the increase of food will at least keep pace with the increase of population. The writers also enter an urgent plea for a more complete statistical study which would give facts of age distribution, fertility, mortality in relation to social conditions and so forth.

P. J. B. H. E.

MAXSON BIRSE, P. *Scottish Pioneers in Tropical Medicine*. *Edinburgh Med. J.* 1948, Apr. v. 55, No. 4: 223-31.

An interesting series of biographical sketches of some of those who have attained to fame in tropical medicine after medical training in one or other of the Scottish centres of learning, Aberdeen, Edinburgh and Glasgow. Sir Philip starts with James Lind who lived through the greater part of the 18th century and is known mainly for his work on scurvy and the diseases of seamen. (There was another James Lind contemporaneous with him who also served in warm climates and is often confused with the former. More than a score of eminent tropical pioneers in medicine are spoken of—Crainger and the dysenteries, Wright and yaws, Livingstone and head, Chubbald the parasitologist, Pinkerton the first lecturer on tropical medicine at Edinburgh, Timothy Lewis and D. D. Cunningham friends and colleagues and both Fellows of the Royal Society. Lewis has been called the Godfather as Maxson the Father of Tropical Medicine. So to more recent times to men but later with us and known to present-day Fellows of the Royal Society of Tropical Medicine and Hygiene: Cantlie, Lenham, Alcock, and, lastly, to those whom we fortunate to meet in the flesh today: G. Carmichael Low whose world-renowned experiences in the Roman Campagna are known to all, Professor H. T. Leiper, helminthologist of worldwide reputation for his work and discoveries on Loa loa, Guinea worm and schistosomiasis, or Malcolm Warren memorable for his work on malaria and species sanitation and the first Director of the Ross Institute.

The article itself begins with a quotation from Longfellow's *Psalms of David* and, not so aptly, ends with a misquotation from the same poet: "The heights by which men are led and kept—the author being perhaps led away by the example of Scotland's national poet who rhymed 'Luch Luchard with' also ye."

H. H. H. H. H.

## BOOK REVIEWS

SCHAPER, I [Professor of Social Anthropology, University of Cape Town]  
**Migrant Labour and Tribal Life A Study of Conditions in the Bechuanaland Protectorate** pp vi+248, 1 folding map 1947 London New York  
 Cape Town Geoffrey Cumberlege, Oxford University Press [18s.]

For the past seventy years or more, Africans of Bechuanaland have been leaving their homes and the influence of tribal life to work in the Union of South Africa, a very large proportion to be employed on the Kimberley or South-West African Diamond Fields or the mines of the Witwatersrand. Except in the tsetse-infested Okovango swamp area of the north-west, the scarcity of surface water is the chief single natural difficulty to be combated by the African cattleman and farmer of Bechuanaland, this scarcity is extreme in the 135,000 square miles of Kalahari Desert in the west and south-west. The small population of this desert area consists essentially of Bushmen with an admixture of Bantu blood, of Bantu stock the Tswana are the dominant group and form the ruling communities of all the principal tribes inhabiting the more fertile eastern districts along the boundaries of the Transvaal and Southern Rhodesia, amounting to some four-fifths of the total population of 250,000—with a density of 3.9 persons per square mile. Water shortage and primitive agricultural methods make life hard for the Bechuana and it is not surprising that men are readily attracted to industrial work with its regular wages, a migration which in 1913 amounted to 35 per cent of male adults, one third of these were enlisted in the military Pioneer Corps.

The economy of the Bechuanaland Protectorate must be seriously affected, tribal authorities complain that the welfare of the people is suffering, herding of cattle is difficult, farming is incomplete and inadequate—these effects are counterbalanced at least partially, by cash income received from the migrants. In addition, ancient tribal institutions have been affected by the activities of a European administration, by missionaries and by traders. Observations have been recorded on the spread of disease, notably tuberculosis and syphilis introduced from industrial areas, on decay of tribal discipline, on laxity of sexual morals and on an apparent decline in the birth rate.

What of the effect on the migrant personally? Physical results will depend on his environment. On the mines he has to work hard, but in return is looked after in many ways—he receives, for example, a balanced diet and free and immediate medical attention with consequent improvement in physical condition—this is not sustained, unfortunately, when he returns home. In other occupations especially where food and quarters are not provided health is more likely to suffer than to improve, mainly because of an unbalanced diet and insanitary surroundings. The illiterate Bechuana is little affected mentally by his sojourn in the industrial areas and on return to his country slips back readily into his previous and traditional mode of life with perhaps some resentment of tribal authority or discipline. The partly educated Tswana on the other hand may get a relatively good job away, and returns home with a broader outlook and is generally a more useful member of his tribe. Some remain away permanently and are 'lost' to their tribe.

Though this book is of interest mainly to South Africans the material presented covers the impact of highly organized and rapidly progressive European industrial undertakings on the economically self-sufficient African inhabitants of a vast bounding territory over a period of sixty years. The objective detail of methods, causes and effects of migration makes most interesting reading and should prove valuable to those whose duty it is to watch the interests of the African tribal area and to the residents of

Britain who for political or business reasons is interested in the development of East and Central Africa. The final chapter deals with some possible remedies bearing in mind that Bechuanaland is only one of many sources of African labour for South African and S. Rhodesian industry.

Detribalization is not inevitable and every encouragement should be given to the maintenance of contact between migrant and home by improved organization at the site of industry by contracts which permit of regular return home and by ease of transportation. Most important of all is the alleviation of the difficulties of life of the general population and the coincident encouragement of a larger proportion of males of the 20-40 age group to remain in their home territories by improvements in the administration, medical education, health and welfare services and methods of agriculture and animal husbandry. Restriction by statute of the numbers of migrants is not recommended.

This book is the outcome of a request by the Bechuanaland Protectorate administration to the author to study the effects of labour migration on tribal life and contains useful statistical information in eight appendices and forty-three tables.  
R. Ford T. Cole

UNITED STATES PUBLIC HEALTH SERVICE AND TENNESSEE VALLEY AUTHORITY  
Malaria Control on Impounded Water pp. xiii+422, 15 figs. 1947  
Washington D.C. U.S. Government Printing Office

The Tennessee Valley Scheme vaguely reminds most people of the New Deal and the development from a primitive to an advanced state of a large tract of land. To malarialogists, it is one of the foremost examples of ambitious malaria control, in its way unique and the Mecca to which they turn when they reach the United States. Vast water conservation, irrigation and hydroelectric works have been created in a potentially malarious country where the principal vector, *Anopheles quadrimaculatus*, chooses the edges of impounded waters as a preferential breeding place. The necessity for malaria control has been recognized from the start and it has been integrated in the engineering works as an essential part of the scheme. Success has been complete and by 1945 a potentially epidemic year only 20 out of 15,338 blood films taken from inhabitants in 1943-1944 were positive (see this Bulletin 1947: 44-81).

For the first time the methods used are fully described in a book prepared under the direction of Dr E. L. Bishop and M. H. D. Hillis and edited by Mr C. J. Mansur. To some extent the title is inadequate for it deals at length with the morphology, bionomics and ecology of the North American anophelines, the parasitology and epidemiology of malaria and the conduct of malaria surveys, as well as malaria control by all established methods except drug prophylaxis. It thus constitutes a complete textbook of malaria control under American conditions whatever the ultimate origin of the vector might be.

The chief interest to the non-American reader lies in the first half of the book which deal with the management of impounded water on which it constitutes an authoritative statement such as is not available elsewhere. There is a well illustrated and fully detailed account of every process in the prevention of mosquito breeding from the time of the first decision to create a reservoir through its construction to the time of its routine patrol.

When a reservoir is first projected detailed maps are prepared showing the probable extent of anopheline breeding, around its perimeter any necessary changes in the original plan are then made and a control scheme outlined for every foot of water edge. Usually the first step is clearing and drainage of the margin to give swamp water edge leaving no emerging terrestrial vegetation on the shore to be flooded, a clear stretch above the normal water line where the

flotsam carried by floods can be stranded without embarrassment to subsequent control, special provision for the stranding of debris in some areas, and no hollows likely to hold water above normal water line on the subsidence of floods. On formation of the dam, the main object is to keep clean shore lines, mainly by water level management and plant control. During the mosquito season a regular cycle of fluctuation in the water level is followed and discourages breeding both through its direct action on larvae and its indirect effect on the vegetation which is essential to them. The cycle varies with the type and function of the reservoir, some types being less discouraging than others, but in all cases it produces a marked reduction in breeding and in the need for

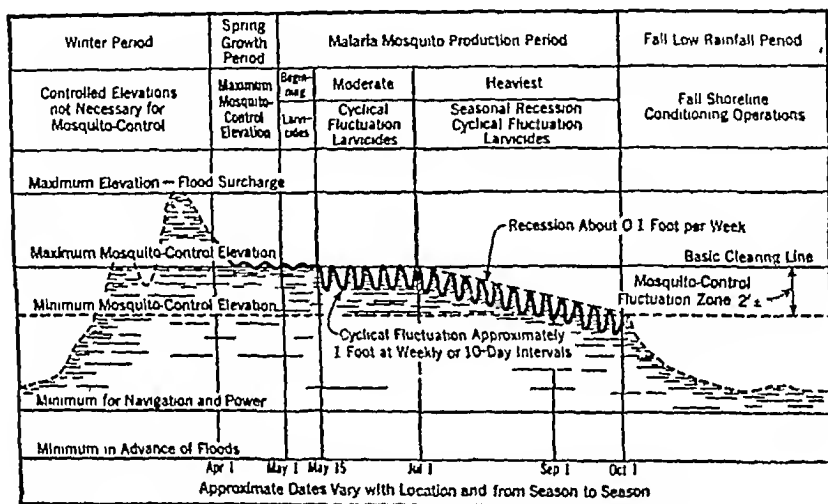


FIGURE 50 —Desirable phases of water level management for mosquito control on main river reservoirs.

[Reproduced from 'Malaria Control on Impounded Water']

larvicides. Plant growth is modified by many methods, including, besides water-level-management, the use of selective hormone and conventional herbicides, the management of grazing, mechanical clearance and others which are fully described.

Where these measures are inadequate, larvicides are used, mainly DDT. Most are applied from aircraft, and the book gives a good account of air practice, but all varieties of mechanical, semi-mechanical and hand distribution are used from the shore and the water. As prevention of breeding may be temporarily either impossible or uneconomic, control measures extend to the mosquito proofing of houses and the application of indoor residual insecticides.

The book is well got-up and both freely and ably illustrated with sketches, plans and photographs, coloured where that is helpful to their interpretation, there is no phase of mosquito control which it does not cover in an able manner. Though written with the object of illustrating American technique and referring only to American anophelines it is a text book of malaria control which will be of great value wherever the English language is read. The reviewer's sole criticism is perhaps ungenerous as it is one of excessive modesty. The Tennessee

Valley Scheme is nowhere described as a whole entity. Though every method used on it is given in full one could read the book unaware of its scope, of the organisation involved in a work of this magnitude, or of the relative importance of the different measures in the whole scheme. Even the few elementary facts at the start of this review have come from the reviewer's general knowledge and he still wonders what are the complications involved in treating 10,000 miles of shoreline.

G. Macdonald

AMARAL, A. Dácio P. PONTES, J. Fernandes & PIRES, Carlos D. de Avila. Amebíase. Estudo etio-patológico, clínico, terapêutico e epidemiológico. [Amoebiasis. A Pathological, Clinical, Therapeutic and Epidemiological study.] 355 pp. 48 figs. 1947. S. Paulo: Tipografia Rosalillo Rua Rui Barbosa V. 333.

This work originated in a study of Intestinal Amoebiasis in Brazil to be followed by a report of more work on the medico-social problem of amoebiasis. The present volume is the outcome of a collaboration between the departments of parasitology and clinical medicine of the São Paulo University and the medical officers in charge of the penitentiary and the gastro-enterological clinic of Santa Casa.

After an introductory chapter in general terms, there follows the first part dealing with the parasitological aspect starting with the story of the discovery of amoebae in man, *E. gingivalis*, by GROS in Russia a century ago (1849) and *E. coli* by LEWIS and CORNINGHAM in cholera stools in 1870-71 and of LÖSCH's amoeba in dysentery in Russia (1875) though Lösch did not recognise its pathogenicity. KOCH (1883-87) and HARTMANN in Egypt (1884). Yet it is considered the pathogenicity or non pathogenicity of various amoebae—*E. coli*, *E. histolytica*, *E. dispar*, *E. m. m.*, *Endolimax nana*, *Iodamoeba butschlii* etc.—and there follows a long discussion on nomenclature and an account of the morphology and biology with good illustrations and graphs indicating the sizes of the cyst forms. A subsection of this part is concerned with the action of the amoeba on man, with a setting out of the different views regarding its pathogenicity and the results of animal inoculation, bearing in mind that some laboratory animals may be naturally infected by amoebae. The statements in this chapter as indeed throughout the work are well documented and illustrated by quotations in the original.

Part II considers the pathological anatomy with very fine reproductions of the lesions in various organs of the intestine large, small and appendix and the presence of granulomata (amoebomata) also in the liver infected in being brought there by the blood stream, by the lymphatics (not admitted in some writers) by the peritoneum, and by direct extension in the lung by continuity and by embolism and in the brain.



others passing cysts but presenting no other symptoms. They quote Craig as saying that constipation is a frequent symptom in carriers, in fact, the rule rather than the exception, and cases are quoted in support of this. In this section also observations and comments are made on hepatic and pulmonary amoebiasis.

Part IV, *Diagnosis*, takes up the methods in turn. Direct examination, culture, animal inoculation, sigmoidoscopy, with records of cases, complement fixation with an aqueous extract of faeces or of pus from a liver abscess in an experimental kitten, or Craig's alcoholic antigen, or Stone's cyst antigen, the intradermo-reaction with mucus and fragments of intestine in saline from a case of acute dysentery, by radiology revealing local spasm. A table is given, adapted from Craig and Faust, for distinguishing the cysts, in Lugol's iodine or stained by iron haematoxylin, another table from the same authors gives the distinguishing features of the six amoebae mentioned above, stained and unstained. The authors record that in examination of 2,727 samples of faeces 220 were positive, the numbers at successive examinations being 115 (52.2 per cent), 41 (18.6), 29 (13.1), 16 (7.2), 15 (6.8) and 4 (1.8).

Part V, on *Treatment*, begins with a general survey of the indications and then speaks in more detail of (1) Alkaloids—*kurchi*, cinchona, *Chaparro amargosa*, and ipecacuanha derivatives. (2) Quinoline derivatives—*yatren*, *vioform*, *diodoquin*. (3) Arsenicals—trivalent (606 or *sanluol*, and 914, *neosalvarsan*) and pentavalent (*treparsol*, *stovarsol*, *carbarsone*). (4) Others—liver, liver extracts, cod liver oil, E B I, *adrenaline*, bismuth salts, etc. Lastly dietetic treatment. The authors give the views of others and then their own, stating that they place most reliance on emetine, but stressing that to be successful it must be given early, intensively, intermittently and periodically.

The sixth and final part considers *epidemiology and prophylaxis*. A map on a very reduced scale, but nevertheless fairly clear, of North and Central America shows the districts affected and there is a table quoting the incidence figures in the eastern hemisphere as recorded by various authors. There is another map of South America and a table giving various records of the names of investigators, the number of examinations carried out by them and the number found positive, in Canada, different parts of the U.S.A., South America and the West Indian Islands. Another map, on a rather larger scale, indicates the parts of Brazil where investigations on prevalence have been carried out and the results recorded by observers in the different States are quoted. Thus, in São Paulo alone 35 records are quoted in which the numbers examined ranged between 18 and 5,429 and the percentages positive between 0.1 and 50.39. Though detailed, these figures are not very informative. For example, one figure of 38.8 per cent positive is based on examination of only 18 apparently healthy persons and the 50.39 on 127 believed to be healthy. The highest number examined, 5,429, were of specimens sent to the laboratory in the Capital District as long ago as 1917, and among these only 10 per cent were positive. The question of age incidence is referred to, but here again little can be learned, because the records are based on very few cases and in limited localities. Nothing new is said on the mode of conveyance or on prophylaxis and both are dealt with in a few pages.

To sum up. The information in this book is well set out, interestingly expressed and clearly printed. To have accomplished such a task of collating information and assimilating to it their own investigations must have demanded wide research and it is most useful to have all these facts brought together in a single volume. The sections are well balanced, none being given disproportionate space. The clinical cases detailed, though few, have been carefully selected—they might be increased with advantage. References number nearly 500 from more than 250 authors from all over the world. Full credit has been given to other

workers in this field. In short this is a book which should certainly be at hand for reference by anyone interested in the subject of amoebiasis.

H. Harold Scott

VAN THIEL, P. H. [Professor of Parasitology of the University and the Institute of Tropical Medicine at Leiden.] *The Leptospirines*. pp. x+231. 19 figs. on 8 pls. & 5 text figs. 1948. Leiden Universitaire pers. Leiden. {£16.50} [Review appears also in *Bulletin of Hygiene*]

This book is a useful addition to the literature on leptospirosis. It should prove of value both as a work of reference and as a guide to those who have to undertake epidemiological investigations in the field. The clinical side of the various leptospiroses is less adequately covered. The full report of work done in Holland and Indonesia is especially welcome because much of it was not readily available to English readers.

After a chapter on the morphology of leptospires the unitary and pluralistic views on the species problem are discussed. On the epidemiological and experimental evidence the author accepts Schillinger's classification—“special” types are ranked as species if more or less sharply defined differences exist in (1) antigenic structure (2) epidemiological behaviour with respect to carrier hosts (3) behaviour in experimental animals (4) geographical distribution (5) clinical characters of disease produced in man. This outlook has practical advantages. If serum treatment is employed the specific serum must be administered. This would be impossible if the diagnoses were merely “leptospirosis”. Preventive measures too may vary according to the carrier host.

The third chapter contains full details of the laboratory methods required in the isolation culture and serological identification of leptospires. Criticisms are made of the different methods and suggestions are made to the appropriate occasions for their use. This chapter is particularly valuable. The information it contains was scattered throughout the literature in a number of languages, and has never before been brought together.

Epidemiology is the subject of the next chapter. Infection by direct contact with urine containing leptospires is not common, except perhaps in the case of *L. canicola*. Attention is therefore directed mainly to the means by which water is contaminated by carriers, to the conditions necessary for the survival of the organism, and to the most likely method of infection in man. Techniques are described for isolation in urine, and leptospires are inspected with

Prophylaxis is considered shortly under (1) Destruction of leptospires by drainage of slumps or altering the acidity of waters when practicable, though the use of calcium cyanamide as a fertilizer proved futile in the rice fields in Japan. (2) Destruction of carriers and growing of buildings and swimming pools against it. (3) Protection of person at risk by the wearing of rubber boots and gloves or prophylactic vaccination.

Chapters on the pathological and biochemical changes and on the symptomatology in man complete the general part of the book. The method of presentation was doubtless used to advantage in later editions. It may be the best possible but the result is not very felicitous. The manifestations of leptospirosis as well as severe and the benign forms differ so widely from the seric varieties that the reader is left without any clear clinical pictures.

In the second half, each leptospire is considered individually, special attention being given to epidemiology and experimental studies in animals.

The symptoms of the diseases in man receive relatively little notice, but the other aspects are very well treated

The book is well written and produced, but lacks a subject index

*J C Broom*

LEMIERRE, A *et al* [Edited by] *Traité de médecine, Vol 2 Maladies infectieuses (seconde partie) Maladies parasitaires* [Treatise of Medicine - Vol 2 Infections and Parasitic Diseases] 955 pp, numerous figs 1948 Paris Masson et Cie, 120 Boulevard Saint-Germain [1,950 fr, £2 10s 0d]

The second volume of this Treatise of Medicine, which is a very considerable work of seventeen volumes, deals partly with infectious diseases [most of which occupied the first volume] and largely with parasitic diseases. About 700 of its some 1,000 pages deal with diseases due to parasites and fungi and those caused by bacteria or viruses which might properly be called tropical diseases. These are dealt with systematically and, in the case of some of the more important diseases, at considerable length. Historical, geographical, epidemiological, pathological and clinical aspects are dealt with, transmission and vectors are discussed, and diagnostic, therapeutic and prophylactic methods described.

There is a noticeable variation in the emphasis on the different conditions and their features. For example, the chapter on malaria occupies over 80 pages which cover the subject widely and include references to recent (but not the most recent) work on the exo-erythrocytic stages of the parasite, on the other hand, although there is a brief reference to the drug SN 7618, there is none to paludrine. Again, there are 35 pages dealing with epidemic typhus and 5 with murine but mite-borne typhus only occupies a page and a half and is separated from the typhus group as a subdivision of "exanthemata transmitted by mites or ticks". It would not be reasonable to expect that so tremendous an undertaking as this series of volumes, the preparation of which must inevitably occupy a very long period, should contain the most recent advances in the knowledge and treatment of the diseases concerned. Most of the references are prior to 1945, so that the bulk of the considerable amount of material published since then is not available.

Nevertheless, the volume contains a vast amount of detailed information. There are numerous references, largely in the form of footnotes in the text. The work is fully illustrated with photographs, diagrams, drawings, and a few excellent coloured plates. Many of the photographs might with advantage be reproduced more clearly.

The field is widely covered and there appears to be no tropical condition of consequence which is not dealt with. The volume has been prepared by an imposing team of some 30 collaborators and the list includes a number of recognized authorities whose names will be familiar to workers in tropical medicine.

There is a full table of contents, but the absence of an index in so large and detailed a work is a disadvantage.

*H J O'D Burke-Gaffney*

HUBBARD Clarence Andresen [Formerly Head of the Department of Biology and Director of the Pre-Medic Curriculum, Pacific University, Forest Grove, Oregon] *Fleas of Western North America Their relation to the Public Health* pp ix+533, numerous illustrations 1947 Ames, Iowa Iowa State College Press [36s]

The great part of the book consists of a taxonomic consideration of the fleas known to occur in North America west of the hundredth degree of longitude.

This is prefaced by general introductory matter including an account of the relation of these insects to public health, and followed by host indices and so forth.

Such a work might well be solid but tedious. The author has been successful in killing this, and in communicating some of his own personality and enthusiasm. He leads off with an account of the work and personal careers of three pioneers, C. F. Baker, Nathaniel Charles Kothschick and Earl Jordan, the last two of whom are described as "the inseparable English duo." The author then sweeps on to the period following the introduction of plague to California in 1900 and writes of new workers who were attracted to the study of the entomology of the disease. From that point he continues right on to 1944 mingling entomology, personal notes, photographs of workers and references to plague in the area. A section on the medical importance of these insects follows. It deals mainly with plague and describes what has occurred in the States of Western North America. It seems that in North America as a whole since its inception into man in 1900 there have been 506 human cases with 341 deaths. On a later page the author puts together all the records of the recovery of *P. pestis* from rodents in North America. One notes that the bacillus has been recovered from members of eighteen of the thirty genera of rodents.

The author then passes on to deal rather sparingly with typhus but here we feel that he is not on sure ground for he distinguishes fundamentally between the typhus of the Old World and of the New and regards murine typhus as a characteristic disease of the New World only. He then reviews our knowledge of the infection of fleas with *Brevella tularensis*, a matter on which North American workers have made most valuable contributions. The introductory section is concluded with paragraphs on fleas as pests of house or farm and on the development of allergy towards these insects. This is followed by practical chapters on trapping small mammals, the technique of mounting, and the external anatomy of fleas with special reference to identification. One notes that in several places in this text the author recommends kerosene as an insecticide and suggests that one should kill flea larvae by watering them with salt water.

The systematic part of the book runs to more than 300 pages and follows conventional lines. It includes not only the distinguishing anatomical characters of each species but data on biology and seasonal and geographical distribution within Western North America. The host records seem to be very full and in nearly every case the species of host is given a Latin name, an excellent point. One notes that *Tunga penetrans* is listed because of its possible future importance though it has not yet been identified in the area. *Cimex lectularius* is common and widely distributed and occurs on many species of hosts including wild carnivores. *Cimex phylloides* fast is a serious nuisance to man in summer and early autumn, and some hosts which become sensitized. It is suggested that they should be treated with flea antigen. *Xenopsylla cheopis* is recorded from several Western States and British Columbia.

The last part of the book lists the 46 species of flea known to occur in Western North America and shows their currents in the separate States (California with 102 species leads the list). A similar index is given of the distribution of 156 species of fleas unknown to the West in the Eastern States. There are then a total of 371 species in North America (including ten introduced from the Atlantic and the Pacific Coast). A valuable feature of the book is the "host index" which not only lists in detailed order (in full the work of hosts and all lists in relation to groups including man) on which fleas have been found in the area, but each of these host groups there is a page or two of notes on biology of the species of fleas found on that host. The bibliography gives a continuation of that published by Jensen and Brown (1937).

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# Book Reviews

The book contains an immense amount of local information and will be valued by specialists. The English is often prolix but the author's meaning can be made out. The proof-reading has not been completely successful.

P A Burton

JETHIER, Vincent G [A.M., Ph.D., Professor of Zoology and Entomology, Ohio State University, etc.] *Chemical Insect Attractants and Repellents* PP vi+289, 69 figs 1947 London H K Lewis & Co Ltd

The author feels a natural dissatisfaction with the present state of our knowledge about substances which are attractive or repellent to insects and about their mode of action. He has gathered together a large body of empirical foundation for an improved understanding of the subject.

The book covers a wide ground and represents much reading. The author opens with general chapters which give some idea of the type of response that may be observed when insects are exposed to physical stimuli such as odours or humidity. The insect's reactions to stimuli of this type are related to its needs for food, attraction to members of the opposite sex, recognition of members of its own species, discovery of a place in which to lay eggs, and so forth. This is followed by several chapters giving information on the reactions of insects to certain groups of chemical stimuli, e.g., the essential oils, products of fermentation, substances that result from the decomposition of fat, protein, etc. The author also gives attention to physiological methods and apparatus by which one may study and compare these responses. In dealing with baits and traps, the subject is considered generally. The author has wisely omitted a mass of empirical formulae and has not discussed the detailed relation of this type of work to the control of insect pests.

In passing over from attractive to repellent substances, the author reaches a part of his work which is of more immediate interest, perhaps, to the readers of this *Bulletin*. There are sections dealing with repellents against blood-sucking flies, house flies, harvest mites (*Trombicula*) and so forth and these give a good up-to-date account of the subject. It is clear that the author is familiar with both British and American published work. It would perhaps have been welcome if he had felt able to give more attention to the achievements and limitations of some of the most effective repellents such as dimethyl phthalate, Indalone and extracts containing pyrethrum.

The book covers much ground on the borderline between biology and chemistry, the general attitude being careful and scientific. It is hardly possible in the present state of knowledge to discover the principles which may be involved, but the book is likely to be influential in the development of the subject.

P A Burton

DANIELSSEN, D C & BOECK, C W *Atlas de la Lèpre* Bergen en Norvège 1847 [Atlas of Leprosy] (Édition commémorative du centenaire) [Re edited by H C de Souza-Araujo] 1946 Rio de Janeiro

Professor de Souza-Araujo has performed another service to leprologists. He has re edited the Facsimile of Danielssen and Boeck's original *Atlas of Leprosy* and brought it out (in monochrome) in commemoration of the work first published in colour in Norway in 1847. Professor de Souza-Araujo had three objects in view in undertaking this issue. First, to keep green the memory of the two famous Norwegians, Daniel Cornélius Danielssen and Carl Wilhelm Boeck, who may justly be regarded as the founders of modern leprology, second, to help the International Leprosy Association to re-establish, or at

least to re-organize the Boreau and the International Journal of Leprosy at Manila University destroyed by the Japanese in the last war by presenting to it the proceeds—a most munificent gesture as the Professor would doubtless reap a rich harvest from the sale of such a work. His third aim was to make the younger workers in this field acquainted with the sterling work of their predecessors.

The price affixed to the *Atlas* is \$3.00 (U.S.A.) or £1 which should be sent to Dr. Ernest Muir, Secretary-General of the International Leprosy Association, 167 Victoria Street London S.W. 1.

The *Atlas* comprises two portraits of Danielssen and one of Boeck, and 74 black and white plates full page and beautifully reproduced depicting the many forms and stages of the disease. Appended is a facsimile reproduction of the title-page of the original treatise on leprosy or "Elephantiasis des Grecs" as they called it which accompanied the original *Atlas* of coloured plates, published by J. B. Baillière in Paris and J. L. Baillière in London.

Tropical workers owe a twofold debt to Professor de Souza Arai for his thought of bringing out this volume and for the excellence of his accomplishment.

H. H. G. Stott

SCHÖNE RUDOLF *et al.* Internal Medicine, Part I. First Review of German Service 1939-1943. 708 pp. 18 figs. 1943. Published by Office of Military Government for Germany Field Information Agency. Translated British, French, U.S.

This volume written in German is the FIAT series of publications designed to inform international science of research done in Germany during the war years, reviews the work undertaken in connexion with "internal medicine."

Almost half of the 388 pages are occupied by the first chapter which reviews work done on infectious diseases: these include bacillary infections, rickettsial diseases, virus and protozoal diseases with brief references to malaria and infections and general theoretical considerations. This chapter includes brief reference to cholera, some ten pages dealing with typhus and a similar number with malaria and amoebic dysentery. In the last two-thirds the paper deals largely with the wartime localisation and treatment of the diseases.

The remaining six chapters deal with work on diseases of the circulatory, respiratory, digestive and urinary system and with allergy. Each section contains a list of references to the workers concerned, which in their length indicate that much investigative work was undertaken: the descriptions of the work are however necessarily brief.

H. J. O'D. Burke *et al.*

# TROPICAL DISEASES BULLETIN

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## EXO-ERYTHROCYTIC SCHIZOGONY IN MALARIA

By P C C GARNHAM, M D, M R C S, D P H

*Reader in Medical Parasitology, London School of Hygiene and Tropical  
Medicine (University of London)*

Malaria parasites\* undergo four cycles of development (1) the sexual cycle starting with the growth of gametocytes in the vertebrate host and continuing with sporogony in the tissues of the mosquito, (2) the pre-erythrocytic development of the sporozoite, (3) asexual schizogony in the red blood corpuscles and (4) exo-erythrocytic schizogony. The second and fourth stages represent the tissue phases of malaria in the vertebrate host and are the subject of this article. They are still imperfectly differentiated one from another and it is impossible, in many instances, to state where one ends and the other begins. Both phases were unknown until comparatively recently, though GRASSI (1900) in the primary wave of malaria research was forced to the conclusion that there was a third developmental cycle in the body of man, during the incubation period, and that this form would exhibit a special character of its own. He abandoned this opinion when SCHAUDINN apparently demonstrated the direct entry of the sporozoite into the red blood cell.

The theory received little attention for 30 years. JAMES (1931) revived it in order to explain many anomalies in the behaviour of the malaria parasites. He suggested that sporozoites entered connective tissue cells or cells lining the capillary blood vessels and remained there until the cells broke down, 8-10 months later, at the end of the protracted incubation period. RUGE (1936) developed the hypothesis a little further and it was eventually so well supported by accumulating knowledge that there was nearly enough indirect evidence to prove the existence of a tissue phase in human malaria. The evidence included the following points —

1 The chromatin of the sporozoite nucleus is arranged so differently from that of the blood forms that GRASSI (1900) thought that direct development, one from the other, was impossible.

2 Most observers were unable to see the direct penetration of a red blood cell by the sporozoite. [Is there any malarialogist who has not attempted to watch this process under the microscope?]

\* The use of the term malaria parasites in this article is confined to blood protozoa belonging to the family Plasmodiidae. Recent work has indicated that some modification will be necessary in the definition of the families and genera in the sub-order Haemosporididae, and in order to show clearly their relationships a brief account of exo-erythrocytic schizogony in the various genera of the sub-order is included.

3. Quinine has little or no therapeutic action during the incubation period and yet it has a powerful action on the parasites directly they appear in the blood (SERGEANT and SERGEANT 1922).

4. The experiments of FAIRLEY (1945) crystallized the exact nature of the problem. These showed that sporozoites circulated in the blood for about half an hour after inoculation and that they then disappeared. The blood was shown to be non-infectious after this half hour until the end of the incubation period. During this interval in avian malaria (172 hours in the case of *P. cathemeromum*) WARREN and COGGESHALL (1937) had already demonstrated that the circulating blood was non-infectious, the parasites being held in the spleen, liver and bone marrow.

Exactly who first saw exo-erythrocytic parasites in malaria will probably never be known. Among the earliest were MACCALLUM (1898) AXENHUTZ (1910) BEN HARILL (1923) and UGARI (1930) then HUFF & BLOOM (1935). But the first person to have recognized their significance appears to have been RAFFAELLE (1934). He described unpigmented forms in *P. elongatum* infections and suggested (1938a) that the sporozoites of this species developed within endothelial cells. He also found (1936b) extremely scarce exo-erythrocytic parasites in *P. rodicum* infections in the reticulo-endothelial cells of the liver, spleen and bone marrow of canaries, after inoculation with large doses of sporozoites.

The full significance of these findings was not realized at the time and even after 1937 when JAMES and TATE announced the discovery of the highly characteristic E.E. forms in *P. gallinaceum*, not a few (e.g. HIGHER and WOLFSON 1938a) thought these unpigmented parasites were as likely to be *Toxoplasma* as a stage in the development of *Plasmodium*. Confirmation of JAMES and TATE's work, however, rapidly followed, *P. gallinaceum* proving itself an ideal parasite for the elucidation of the whole cycle in avian malaria. The discovery of pre-erythrocytic forms in the incubation period was announced independently in 1940 by LILY MUDROW and by SHORTT MEXON and IVAN and in 1944 HUFF and COLLSTON worked out the full cycle of *P. gallinaceum* in the greatest detail, whilst MUDROW and REICHENOW investigated *P. foveolatum*.

Similar stages were seen in many other avian malarial parasites. In 1944 exo-erythrocytic schizogony in saurian malaria was described by THOMSON and HUFF. Finally in 1948 the tissue phase in mammalian malaria was discovered, first in the monkey parasite *P. cynomolgus* (SHORTT and GARNHAM) and slightly later in the human, *P. vivax* (SHORTT, GARNHAM, COVELL and SHUTE).

Very useful summaries of the subject have been made by GIOVANNOLA (1939) PORTER and HUFF (1940) HEWITT (1940b) and HUFF (1947).

### Terminology

New knowledge of the life cycle of the malarial parasites inevitably required an extension of nomenclature. Definitions of the new terms are given below—

**Pre-erythrocytic schizogony**—This term refers to the development of the sporozoite during the incubation period. It may occupy one generation only as in mammalian malaria, or several generations, as in the avian form. This stage can be said to terminate on the first appearance of parasites in the red blood corpuscles.

**Exo-erythrocytic schizogony**—This was the original term employed by JAMES and TATE (1938) to describe the developmental forms they observed in the brain and other organs of chicks infected with *P. gallinaceum*. It was used indiscriminately for early and late forms. It is desirable to confine the use of



the name to stages seen in the post-patent period, i.e., after the parasites have reached the blood

**Tissue Phase**—This term embraces both pre-erythrocytic and exo-erythrocytic schizogony and is to be used for preference when the exact stage of the infection is unknown

**Phanerozoite**—Any exo-erythrocytic parasite except pre-erythrocytic forms (HUFF and COULSTON, 1946)

**Exo-erythrocytic schizogony** *gallinaceum*-type and *elongatum*-type PORTER (1942) made a useful distinction between two types of schizogony. E.E. development of *gallinaceum*-type occurs predominantly in the lymphoid-macrophage system, including endothelium. E.E. development of *elongatum*-type is confined to the wandering cells of the blood and organs (particularly the haemopoietic system)

**Cryptozoite**—HUFF, COULSTON and CANTRELL (1943) devised this word to denote the first stages in the development of the sporozoite. Cryptozoites are the product of the first division of the sporozoite and are contained in a cryptozoic schizont

**Metacryptozoite**—Following the first cryptozoic generation, are schizonts which produce metacryptozoites and the term (proposed by HUFF and COULSTON, 1944) includes all pre-erythrocytic stages with the exception of cryptozoites

**Micromerozoite**—Certain E.E. schizonts consist of many nuclei and little cytoplasm. These microschorizonts eventually produce a large number of micromerozoites (128 or more in the case of *P. relictum*, REICHENOW and MUDROW, 1943). In size and structure they are like the merozoites resulting from schizogony in red blood corpuscles and they are destined to enter such cells themselves

**Macromerozoite**—The macromerozoites are larger bodies than the micromerozoites. They probably number not more than 64 (in *P. relictum*) within the macroschizont. They do not invade red blood corpuscles, but enter tissue cells

**Megaloschizont**—This term was applied by HUFF (1942) to describe the large schizonts of *Leucocytozoon* in the tissue cells of the heart, spleen, intestine and liver. The mature forms measure over 100 $\mu$  in length and contain thousands of merozoites. They are solid bodies

**Merocyst**—An analogous structure to the megaloschizont is the merocyst (GARNHAM 1947) of *Hepatocystes kochi*. During the exo-erythrocytic development of this parasite the substance of the schizont becomes highly vacuolated. The vacuoles coalesce in a large internal space and this space is bounded by a thick wall containing innumerable merozoites. The merocyst measures about 2 mm in diameter

**Cytomere**—WENYON (1926) defines cytomeres as the intermediate bodies of a schizont which actually produce the merozoites. When a certain number of nuclei have formed, the schizont divides into the same number of individual masses, each with a single nucleus. These are the cytomeres, their nuclei undergo further division, and finally merozoites are budded from their surfaces. Such a clear-cut process is rarely seen in the Haemosporididae but various observers have noted the partial differentiation of the schizont during its growth into separate islands or cytomeres. ARAGÃO (1908) first described the phenomenon in *Haemoproteus*. JAMES and TATE (1938) stated that during the growth of *P. gallinaceum* schizonts, the cytoplasm breaks up into a number of cytomeres on the periphery of which the merozoites are developed on digitiform processes. HUFF (1942) showed that during the formation of the megaloschizont of *Leucocytozoon*, the body became divided into numerous (usually several

occurred rarely in the brain. Multiple infections of cells were seen. FANTHAM & PORTER (1944) also found scanty E.E. forms in penguin malaria, which they described under the name *P. eductum* var. *sphenoides*. MAXWELL (1940) studied a variety of this parasite viz. *P. eductum* var. *minimum*, in canaries. Localization in the brain was common and the presence of large and conspicuous vacuoles in the schizonts was a constant peculiarity in this variety. In tissue culture HAWKING (1946) noted that the merozoites were elongate and sometimes arranged radially around a central core.

MISAIROLIS (1940) account of the development of the parasite of *P. raictum* differs from that of the American workers particularly in regard to the primary place of development which Misairolis states is extracellular resulting in the formation of four merozoites. These merozoites are said to enter red blood corpuscles and start the blood cycle.

*P. calhemacrum*.—This avian parasite is very similar in morphology in all forms to *P. eductum*. Its common E.E. sites are the brain and the liver though in heavy infections unpigmented schizonts may be found in the peripheral blood (in eosinophiles). The early forms have been described by HIXLIT and McDROW (1938 and 1939) and were shown to begin as uninvaded parasites lying in endothelial cells or monocytes. These parasites later underwent schizogony dividing into at least 12 merozoites. The late stages have been described incompletely by many authors—HIGGINS and WOLFSON (1938a) illustrated what were certainly the E.E. schizonts of this parasite though at that time they were not prepared to differentiate them from *P. eductum*. In length they may measure 32 $\mu$  and there may be 100 or more merozoites.

*P. circumflexum*.—This large parasite of the elongate gametocyte group has been studied by MAXWELL and GOLDSTEIN (1939). E.E. schizonts are found in the following organs (in order of frequency)—lungs, brain, spleen, liver, bone marrow, heart and ovaries. The schizonts reach the size of 35 $\mu$  in diameter and the merozoites number at least 170. A characteristic feature is the elongate character of the merozoite. The schizonts sometimes show one or more vacuoles, and two kinds occur, one with lightly staining, and the other with much more heavily staining, cytoplasm. They invade the endothelial cells of the cerebral capillaries and the monocytes of other organs. Pre-erythrocytic stages are unknown.

*P. lephure*.—The pre-erythrocytic cycle of *P. lephure* has been studied by HOFF, COLESTON, LUND and PORTER (1947). Unfortunately the host birds employed by these workers did not appear to be completely suitable for the parasite and many of the E.E. parasites were in an abnormal or degenerated condition. They occur in cells of the lymphoid macrophage system and in fibroblasts and, so far, they have only been recovered from the site of inoculation of the sporozoites in the skin. No constant differences were observed between these pre-erythrocytic forms and those of *P. galinaceum*. In the later stages, exo-erythrocytic parasites are abundant in the capillaries of the brain. Macro- and micro-merozoites were observed by TOSAKI and HAWKING (1947) in infected turkeys.

*P. lurae*.—PURCHASE (1947) and SIBERT (1944) reported exo-erythrocytic schizogony in this parasite of turkeys. The forms are most numerous in the lungs and brain but also occur in the liver and spleen. In the brain infection is so intense that the capillaries are completely occluded. The exact morphology of these parasites remains undetermined and the pre-erythrocytic stages are unknown.

*Other Plasmodia of Small Size*.—The malarial parasites of birds are conventionally classified into larger and smaller species (RUSSELL, WERT and MAXWELL, 1946). Exo-erythrocytic schizogony has been found in few of the smaller species probably because the infections have not been sufficiently

studied BARRETTO (1943) has described, briefly, tissue forms in *P. juxtancleare*. He found them solely in the brain capillaries. The schizonts were elongated structures with 2-19 blocks of chromatin. HEGNER and WOLFSON (1938b) described schizonts in reticulo-endothelial cells from birds infected with *P. nucleophilum*. These infections were apparently mixed with *P. cathemerium* and it seems probable that the schizonts were in reality those of the latter species.

*P. elongatum*—Exo-erythrocytic schizogony in this species follows a totally different course from that of the parasites described above. RAFFAELE (1934) and HUFF and BLOOM (1935) give detailed descriptions of the development of this species, they demonstrated that schizogony occurred in a wide variety of cells, extending from mature erythrocytes to erythroblasts, haemocytoblasts, plasma cells, macrophages and granulocytes. The overwhelming majority of the parasites occur in the red blood cell series, probably less than 10 per cent in other cells. Except for (a) size and number of merozoites and (b) presence or absence of pigment, there appears to be little difference in the character of the schizont whatever cell it may be inhabiting. The essential difference between *P. elongatum* and the other parasites is the fact that exo-erythrocytic stages of the latter are largely confined to fixed tissue cells, while these stages in *P. elongatum* occur only in wandering cells.

The schizonts of this parasite produce 4-30 elongated merozoites which are arranged in a most characteristic fashion, more like the arrangement seen in schizogony in haemogregarines than in plasmodia. They lie in parallel rows or bundles. Pigment is produced only in the polychromatophil erythroblasts, normoblasts and erythrocytes. In the erythroblasts only a small granule of pigment is produced. There exists, therefore, no clear line of differentiation between exo-erythrocytic and erythrocytic schizogony in this species, and even when the former can be distinguished, it presents features which link it closely with the ordinary schizogony of the blood. Thus, the number of merozoites is small, the cycle of development is short (24 hours), there is no differentiation into macro- and micro-schizonts and, finally, there is the absence of any tendency to invade fixed lymphoid-macrophage tissue.

The complete pre-erythrocytic cycle is still to be described. RAFFAELE (1934) found exo-erythrocytic parasites early in infections before invasion of the peripheral blood had begun and he assumed from this that pre-erythrocytic development occurred in endothelial cells.

#### *Saurian Parasites*

Exo-erythrocytic schizogony in American lizards was discovered by THOMPSON and HUFF (1944). It has also been observed by the present reviewer (unpublished work) in the East African skink, *Mabuya maculilabris*.

The cycle in *P. mexicanum* is of considerable interest in that it occurs in both wandering and fixed tissue cells, in other words, it partakes of the characters of both the *gallinaceum*- and the *elongatum*-types of schizogony. The parasites invade basophil erythroblasts, lymphocytes, monocytes, thrombocytes and granulocytes and in such cells the round or oval schizonts produce elongate merozoites, 10 to 40 or more in number. The *gallinaceum*-type of schizogony is seen in reticular cells, endothelial cells of capillaries, littoral cells of the liver and macrophages. There is a strong tendency to invade the true endothelium. In these situations, the schizonts are larger and contain 72 or more round merozoites.

#### *Mammalian Parasites*

Reports claiming the discovery of exo-erythrocytic schizogony in human or monkey malaria have appeared from time to time and there can scarcely be a single worker in this field who has not thought at one time or another that he

has at last found the cryptic forms. Usually on reflection and re-examination, it has been possible to find an alternative explanation, but some claims were put forward and their unreliability has recently been analysed by ANGELLINI (1947). Other workers have described various intracellular bodies, but have regarded them more conservatively (e.g. DECOURT and SCHNEIDER 1938; DUBIN 1947). When the liver schizonts of *P. cynomolgi* were ultimately discovered (SHORT, GARNHAM and MALAMOS 1948) their morphology was so entirely unequivocal that they received instant acceptance and the long search at last came to an end. So far the exo-erythrocytic forms have only been demonstrated in *P. cynomolgi* and *P. vivax*. Recent discoveries in other mammals refer to parasites incorrectly placed in the family Plasmodiidae: they are mentioned briefly later in this article.

The technique leading to the discovery of these forms was as follows. In the monkey it involved the introduction of hundreds of thousands of sporozoites by bite and by the inoculation either of large numbers of the whole mosquitoes intraperitoneally or of the salivary glands intravenously. Seven days later the animal was sacrificed and specimens were taken from every organ and tissue. Sections were stained and examined and the schizonts were eventually found in the liver material. After this, it was an easy matter to repeat the experiment in man with *P. vivax* and to extract the necessary tissue by liver biopsy.

*P. cynomolgi*.—Pre-erythrocytic schizogony of this species has been described by SHORT and GARNHAM (1948b) and by HAWKING, PERRY and THURSTON (1948). The process takes place in the parenchymatous cells of the liver and probably only one generation is involved. The earliest forms were seen on the fifth day after infection. They are spherical or oval bodies about  $10\mu$  across and contain about 50 pieces of irregularly shaped chromatin lying throughout the granular cytoplasm. A characteristic of this stage is the very sharply cut margin of the parasite. Growth continues and maturity is reached about the eighth or ninth day. During this time a few curious vacuoles develop in the parasite and indentations of the periphery occur, sometimes resulting in the formation of one or more lobose arms. Nuclear multiplication continues and eventually nearly a thousand merozoites are formed. Each merozoite consists of a small fragment of chromatin on one side and a fairly dense piece of cytoplasm on the other giving the appearance of a "solid ring," a little over  $1\mu$  in diameter. The mature schizont itself measures about  $35\mu$  in diameter. Exceptionally forms as large as  $60\mu$  are to be seen.

After the rupture of the schizont and the escape of the merozoites into the sinusoids, invasion of the residual mass by phagocytes occurs. These cells are lymphoid-macrophage cells, plasma cells and polymorphonuclear leucocytes.

Persistence of the tissue cycle in the liver parenchyma has recently been demonstrated by SHORT and GARNHAM (1948c). Schizonts were found 3½ months after the original sporozoite-induced infection and after months' latency when parasites were absent from the peripheral blood. Schizonts were extremely rare: they resembled pre-erythrocytic forms in most respects, a possible difference being that the younger (3-day-old) parasites appeared to possess a well-defined, very limiting membrane. There is little doubt that these schizonts represent the tissue forms. They presumably continue to develop in the liver throughout an infection, producing showers of merozoites which, however, are normally destroyed by the immune mechanism. Something, upsets immunity: the merozoites are then able to continue the erythrocytic cycle and relapse ensues.

*P. vivax*.—The E.E. schizonts of this species resemble those of *P. cynomolgi* very closely. Oval plasmodial masses develop within the parenchymatous cells of the liver. These exhibit vacuoles, indentations of periphery and

nuclear multiplication, resulting in the formation by the seventh day of a fully mature schizont with 800-1,000 merozoites. The size of the schizont is, perhaps, rather larger than in *P. cynomolgi*, about  $42\ \mu$  in diameter.

*Exo-erythrocytic Schizogony in the Haemoproteidae*

The following genera are recognized in this family, *Haemoproteus*, *Leucocytozoon* and *Hepatocystes*. It is probable that the family will have to be widened to include the malarial parasites of the bat, flying fox, sitatunga and other mammals, these also are considered briefly in this section. All the members of this family exhibit gametocytes only in the blood stream. The Haemoproteidae show affinities not only with the Plasmodiidae but with various genera in the Theileriidae. "Koch's blue bodies" of *Theileria parva* bear a strong resemblance to the E E forms of avian plasmodia and halteridia, and the cycle of the newly described piroplasm, *Cytauxzoon sylvicaprae* NEITZ and THOMAS (1948) of the Duker shows an even closer relationship.

*Haemoproteus* was shown by ARAGÃO (1908) to undergo a tissue phase in the endothelial cells of the blood vessels of the lungs and other organs of the body. Segmentation into cytomeres occurs, each of these continues to grow and eventually enormous numbers of merozoites are produced, enclosed by fine cyst walls. These forms reach  $60\ \mu$  in diameter, and smears show that the cytoplasm has a meshed structure with fairly numerous vacuoles and many nuclei. WENYON (1926) noted that cytomere formation was not inevitable but that the schizont—a large sausage-shaped body—might give rise directly to merozoites. These schizonts may collect in groups in the organs, e.g., liver or spleen, separated from each other by walls of indeterminate origin, the whole focus measuring several hundred microns in diameter.

*Leucocytozoon* E E schizonts were described by HUFF (1942). Two types were found, one occurring in parenchymatous cells of the liver, causing little alteration in the cell, and the second, the megaloschizont, in the heart, liver, spleen and intestine. The megaloschizonts are formed from numerous cytomeres which eventually give rise to extremely numerous bacilloid merozoites, arranged without order in the schizont. These forms may be as long as  $105\ \mu$ . It is probable that the megaloschizont develops within macrophages and also in cardiac muscle cells. These cells become enormously hypertrophied and the nuclei also enlarge.

*Hepatocystes kochi* (a parasite of the lower African monkeys) has recently been studied by GARNHAM (1948) and details of its exo-erythrocytic cycle were elucidated. Development proceeds in the parenchymatous cells of the liver, first as a minute round body, then as a sphere with peripheral nuclei, the nuclei later multiply and become scattered throughout the cytoplasm. The surface of the parasite shows multiple invaginations, vacuolation occurs and the fluid accumulates in a large central vacuole which expands to form the merocyst. Further division of the nuclei has continued in the meantime, possibly with the formation of cytomeres. Eventually the merozoites collect in enormous numbers in the wall of the merocyst, which ruptures and the majority of the merozoites escape into the circulation where they grow into gametocytes. The mature merocyst measures up to 2 mm in diameter. These E E forms persist throughout the infection, discharging a stream of gametocytes into the blood.

A similar parasite has recently been described by RAY (1948) from the Himalayan flying squirrel. It has an E E cycle in the liver resembling in many ways that of *H. kochi* though the cysts are multiple.

*Malarial Parasites of Bats*—MER and GOLDBLUM (1947) found that the bats (*Myotis myotis* and other species) of Palestine, harboured a blood parasite which underwent intense schizogony in the reticular cells and the granulocytes of the

bone marrow. E.E. forms were also present in the wandering and fixed macrophages of the lung, kidney and liver. The parasites in the liver measure little more than  $8\mu$  in diameter. They are of course unpigmented and they produce a relatively small number of merozoites. Ectoparasites of the family Nycteribiidae infest these bats and it is claimed that the glands of one fly contained sporozoites.

Another interesting parasite of bats (the fruit bat—*Myotis Gould*) was studied by MAXWELL (1946) in New Guinea. In addition to gametocytes he found a fair number of unpigmented schizonts in the peripheral blood and these schizonts were all extracellular. They contained a variable number of merozoites and were said to resemble the E.E. forms of avian malaria. It is possible that these bodies in reality were detached portions of a ruptured merocyst. They are not unlike the structures which SCHWARTZ (1933) described from the peripheral blood and bone-marrow in *H. lachrymans* infections. It is doubtful whether they should be regarded as the mammalian equivalent of *P. elongatum* because although in the blood, they lie free and are not in cells of the haemopoietic system.

### Biological Significance of E.E. Schizogony

The conclusion that E.E. schizogony was an essential part of the life cycle of malarial parasites was accepted by most workers after the early work of James and others. Because of its erratic and cryptic nature however some people at first were unwilling to accept this interpretation and they put forward several theories. BRUNER (1937) suggested that the phenomenon might represent an accidental histotropism caused by the unfavourable action of the blood on certain merozoites escaping from the ordinary blood schizonts. CHORRIS (1938) thought that E.E. schizogony was not a normal developmental stage but appeared as the result of loss of function of the reticulo-endothelial cells. These cells start phagocytosis of the parasites but are unable to complete the process and the parasites then continue their own development. CORRAVEITI as late as 1941 regarded the presence of E.E. forms as a sort of accident in the life history of malarial parasites, occurring in only a few species. He also thought that development in histiocytes was not undergone by protozoa. The same worker (1947) stated that the extent of the process depended upon the degree of balance between host and parasite—in other words upon immunity. His experiments had shown that when sporozoites or suspensions of tissues containing E.E. forms were inoculated into clean birds E.E. forms easily appeared—because there was no immunity. If however the inoculation was made into birds in the latent phase of a homologous infection no E.E. forms appeared.

Further knowledge particularly in regard to the tissue phase in mammalian malaria, has made it clear that ex-erythrocytic schizogony is a normal part of the cycle of probably all the malarial parasites just as it is in all members of the Haemosporididae. Variation in incidence as well as the are no greater than similar fluctuations in the number for instance of gametocytes, and as is well known, certain strains of parasites can become unipigmented and permanently gametocyte free. It is now clear that the sporozoite inoculation proceeds to certain sites the exact location of which depends on the species and there develops through one or more generations an infection which produces blood infection, merocytosis. These forms may persist in the original site or elsewhere in the body or they may migrate. It is possible that in the incubation period they develop directly from blood schizonts of erythrocytic forms may develop directly from blood schizonts of

HAWKING *et al* (1948) go as far as to speculate on the phylogenetic relations between the malaria parasites and allied protozoa belonging to the Eimeriidea, based on their common development in intestinal epithelium (*e g*, *Schellackia*) or in hepatic epithelium which is embryologically derived from the former (*e g*, *P cynomolgi*, *H kochi*)

There are still many gaps in our knowledge of E E schizogony. The morphology of this stage is incompletely described, although novel methods have been devised to study it. SHORTT, MENON and IYER (1940) used inoculation into the chorio-allantois of the fowl embryo to observe *P gallinaceum* infections, HAWKING (1944) and more recently GRAMICCIA and BLACK (1948) have employed tissue culture as a means of studying E E forms. The behaviour also of these parasites is only partly understood. E E forms are present in some strains of a species and yet may be completely absent throughout hundreds of passages in another, as HEWITT (1940a) found in *P cathemerrum*. On the other hand, growth in tissue culture may produce a strain which results in infections of an exclusively exo-erythrocytic nature, this peculiarity being maintained unchanged through many subsequent passages (LEWERT, 1948). The development of E E stages in different hosts has been studied by HUFF, COULSTON, LAIRD and PORTER (1947), they showed that *P lophurae* exhibited most numerous E E forms in young turkeys, pheasants and canaries, but few in guinea fowls, on the other hand, pre-erythrocytic forms were commonest in guinea fowls and less common and more abnormal in morphology in chickens, turkeys and ducks.

The infectivity on sub-inoculation of organs containing pre-erythrocytic parasites shows certain peculiarities which at present are not understood. In avian malaria, subinoculation is always successful, in mammalian, it never is. In this respect, the mammalian plasmodia behave like the Haemoproteidae whose asexual stages are only slightly infective (COATNEY, 1933). The failure to infect may be due to the localization of the parasites in special cells (*e g*, hepatic parenchyma rather than undifferentiated endothelium) or it may be because there is probably only a single and lengthy cryptozoite stage in mammalian malaria, with no free merozoites until the end of the incubation period. The chemotherapeutic action of drugs is likely to show corresponding variations based partly on this fundamental difference between the various species. A discussion on this subject is beyond the scope of the present review.

For a long time past, people have felt the need for a reclassification of the malaria parasites. MISSIROLI (1937) suggested the creation of a new genus *Istiocytozoon* for the two avian parasites *P elongatum* and *P gallinaceum*, based on their evolution in reticulo-endothelial cells. This has subsequently proved to be an unsatisfactory basis and the name has been unacceptable to the majority of workers. CORRADETTI (1938) took the opposite view and suggested fusing the two families Plasmodiidae and Haemoproteidae, because the distinction is a purely physiological one referring to the type of host cell parasitized. This interpretation would appear to be invalid because there are gross morphological differences and also, as PORTER and HUFF (1940) pointed out, the two families have distinctive invertebrate hosts. The present position is well summarized by GRAMICCIA (1948) in the statement that a revision of the sub-order Haemosporididae is necessary but cannot be made until many obscure points in the biology and life history of the more important parasites are cleared up. In the reviewer's opinion, taxonomic changes should be postponed until the nature of the tissue phase has been elucidated in (a) *P falciparum* or *P reichenowi*, (b) the small avian plasmodia (*e g*, *P rouxi*), (c) the mammalian analogue of *P elongatum* (possibly the plasmodium of the New Guinea flying fox), and (d) probably certain novelties such as the virulent haemotozoon (*P berghiei*) of the Congo tree rat (VINCKE and LIPS, 1948) and

bone-marrow. E.E. forms were also present in the wandering and fixed macrophages of the lung, kidney and liver. The parasites in the liver measure little more than  $8\mu$  in diameter. They are of course unpigmented and they produce a relatively small number of merozoites. Ectoparasites of the family Ycteribulidae infest these bats and it is claimed that the glands of one fly contained sporozoites.

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The conclusion that E.E. schizogony was an essential part of the life cycle of malaria parasites was accepted by most workers after the early work of James and others. Because of its erratic and cryptic nature, however, some people at first were unwilling to accept this interpretation and they put forward several others. BARNETT (1937) suggested that the phenomenon might represent an accidental histiotrophism caused by the non-specific action of the blood on certain merozoites escaping from the ordinary blood schizonts. CHORIST (1938) thought that E.E. schizogony was not a normal developmental stage but appeared as the result of a loss of function of the reticulo-endothelial cells. These cells start phagocytosis of the parasites but are unable to complete the process and the parasites then continue their own development. CORRADINI as late as 1941 regarded the presence of E.E. forms as a sort of accident in the life history of malarial parasites, occurring, in only a few species, he also thought that development in histiocytes was not undergone by parasites. The same worker (1947) stated that the extent of the process depended upon the degree of balance between host and parasite—in other words, upon immunity. His experiments had shown that when sporozoites or suspensions of tissues containing E.E. forms were inoculated into clean birds, E.E. forms readily appeared—because there was no immunity. If, however, the inoculation was made into birds in the latent phase of a homologous infection, no E.E. form appeared.

Further knowledge, particularly in regard to the tissue phase in mammalian malaria, has made it clear that exo-erythrocytic schizogony is a fundamental part of the cycle of probably all the malaria parasites, just as it is in other members of the Haemosporidia. Variations in incidence occur but there are no greater than similar fluctuations in the number for instance of gametocytes, and as is well known certain strains of parasites can become completely and permanently gametocyte-free. It is now clear that the parasite on inoculation proceeds to a certain site the actual location of which depends upon the species, and there develops through one or more general ones into a schizont which produces blood infecting merozoites. Tissue forms may persist in this organism or else live in the body or they may be so evanescent that after the incubation period, they disappear entirely. With certain species exo-erythrocytic forms may develop as CORRADINI (1941) and others have shown, directly from blood schizonts even from the inoculation of single trophozoites.



HAWKING *et al* (1948) go as far as to speculate on the phylogenetic relations between the malaria parasites and allied protozoa belonging to the Eimeriidea, based on their common development in intestinal epithelium (*e.g.*, *Schellackia*) or in hepatic epithelium which is embryologically derived from the former (*e.g.*, *P. cynomolgi*, *H. kochi*)

There are still many gaps in our knowledge of E E schizogony. The morphology of this stage is incompletely described, although novel methods have been devised to study it. SHORTT, MENON and IYER (1940) used inoculation into the chorio-allantois of the fowl embryo to observe *P. gallinaceum* infections, HAWKING (1944) and more recently GRAMICCIA and BLACK (1948) have employed tissue culture as a means of studying E E forms. The behaviour also of these parasites is only partly understood. E E forms are present in some strains of a species and yet may be completely absent throughout hundreds of passages in another, as HEWITT (1940a) found in *P. cathemerium*. On the other hand, growth in tissue culture may produce a strain which results in infections of an exclusively exo-erythrocytic nature, this peculiarity being maintained unchanged through many subsequent passages (LEWERT, 1948). The development of E E stages in different hosts has been studied by HUFF, COULSTON, LAIRD and PORTER (1947), they showed that *P. lophurae* exhibited most numerous E E forms in young turkeys, pheasants and canaries, but few in guinea fowls, on the other hand, pre-erythrocytic forms were commonest in guinea fowls and less common and more abnormal in morphology in chickens, turkeys and ducks.

The infectivity on sub-inoculation of organs containing pre erythrocytic parasites shows certain peculiarities which at present are not understood. In avian malaria, subinoculation is always successful, in mammalian, it never is. In this respect, the mammalian plasmodia behave like the Haemoproteidae whose asexual stages are only slightly infective (COATNEY, 1933). The failure to infect may be due to the localization of the parasites in special cells (*e.g.*, hepatic parenchyma rather than undifferentiated endothelium) or it may be because there is probably only a single and lengthy cryptozoite stage in mammalian malaria, with no free merozoites until the end of the incubation period. The chemotherapeutic action of drugs is likely to show corresponding variations based partly on this fundamental difference between the various species. A discussion on this subject is beyond the scope of the present review.

For a long time past, people have felt the need for a reclassification of the malaria parasites. MISSIROLI (1937) suggested the creation of a new genus *Istiocytozoon* for the two avian parasites *P. elongatum* and *P. gallinaceum*, based on their evolution in reticulo endothelial cells. This has subsequently proved to be an unsatisfactory basis and the name has been unacceptable to the majority of workers. CORRADETTI (1938) took the opposite view and suggested fusing the two families Plasmodiidae and Haemoproteidae, because the distinction is a purely physiological one, referring to the type of host cell parasitized. This interpretation would appear to be invalid because there are gross morphological differences and also, as PORTER and HUFF (1940) pointed out, the two families have distinctive invertebrate hosts. The present position is well summarized by GRAMICCIA (1948) in the statement that a revision of the sub-order Haemosporidieae is necessary but cannot be made until many obscure points in the biology and life history of the more important parasites are cleared up. In the reviewer's opinion, taxonomic changes should be postponed until the nature of the tissue phase has been elucidated in (a) *P. falci-parum* or *P. reichenowi*, (b) the small avian plasmodia (*e.g.*, *P. rouxi*), (c) the mammalian analogue of *P. elongatum* (possibly the plasmodium of the New Guinea flying fox), and (d) probably certain novelties such as haemotozoon (*P. berghei*) of the Congo tree rat (VINCKE and

the plasmodia of the Canadian bull frogs (FANTHAM PORTER and RICHARDSON 1947) *P. knowlesi* might be added to this list because of certain peculiarities, e.g. its short cycle (74 hours) and its apparent non-transmissibility by mosquitoes. A basis for classification is indicated in the table below which shows tentatively the position of the more important genera and species.

Size of E E Schizonts	Location of E.E. Schizogony	HAEMOPROTEIDAE	PLASMODIIDAE
		Gametocytes only in blood in vertebrate host not a Mosquito	Gametocytes and Schizonts in blood invertebrate host a Mosquito
Macroscopic or nearly so	Endothelium of blood vessels	<i>Haemoproteus</i>	+
	Liver heart, kidney parenchyma	<i>Leucocytozoon</i>	+
	Liver parenchyma	<i>H. pulex</i>	<i>Plasmodium vivax</i> (synonym)
Microscopic	Reticulo-endothelium	<i>Plasmodium</i> sp. of Palestine bats	<i>Plasmodium gallinaceum</i> , <i>Leish. 1c</i>
	Haemopoietic system	<i>Plasmodium</i> sp. of New Guinea flying fox	<i>Plasmodium elongatum</i>
	E.E. and haemopoietic system	+	<i>Plasmodium m. icterum</i>

Re-classification may be required.  
+ Gaps to be filled.

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## SUMMARY OF RECENT ABSTRACTS

### VIII TYPHUS GROUP OF FEVERS

#### *Proteus O\19 type* *Vector house* *and* *fly* *Louse typhus*

**Epidemiology**—STUART (p. 193) shows that louse-borne typhus and louse-borne relapsing fever can exist independently of each other but that when they are related the epidemic of typhus tends to appear earlier by one or more years than the epidemic of relapsing fever.

ANDERSON (p. 58) shows that louse typhus is constantly present in Egypt and that from 1941 to 1944 and perhaps later it was epidemic reaching a peak incidence of 29 per 100,000. In the *Bulletin de l'Off. International d'Hygiène Publique* (p. 197) the point is made that during the period 1939-45 the peak incidence of typhus in Tunisia was in March-May except for 1945 when it was in January. The claim is made that repeated mass vaccination has controlled the epidemic.

ADILLA (p. 197) shows that most of the cases of typhus in Guatemala are of the louse-borne type but that a few have been caused by other vectors.

ANDERSON (p. 703) observed that rickettsiae presumably *R. prowazekii* frozen and dried and sealed under hydrogen were viable after 142 days at -14°C.

ORITZ (p. 195) shows that a protein and stain that are present in organisms contain a constant antigenic constituent. The antigen in *R. prowazekii* and *R. mooseri* present in the supernatant fluid after centrifugation by the culture passes to the cells (ORITZ and H. E. WALKER p. 191).

THOMSON (p. 38) justifies his opinion that the use of the strains of *Proteus* used for tests in the Middle East during the war had become useless by the time they reached the laboratories. Cultures were made and used.

The abstracts in this section are from the *Abstracts of Tropical Diseases* published in 1947 and 1948. The abstracts are given under the names of the authors quoted and the page on which the abstracts are printed.

in ampoules are said to keep indefinitely, and can be used with confidence for making suspensions

In a study of 1,084 strains of *Proteus* in areas free from human rickettsial diseases, WINKLE (p 573) found 12 serological types, including 4 that behaved like X2, X19, XU, and XK The same author (p 574) isolated two strains of *Proteus* X19, one from the blood and one from the urine, of patients with (or suspected of) typhus

WISHART and MALCOMSON (p 194) show that *R prowazeki* and *R mooseri* possess type-specific antigens labile at 60°C, and a common antigen stable at 100°C but destroyed at 120°C The latter contains two factors, one of which is common to *Proteus* OX19 The Weil-Felix reaction, therefore, is a specific immunological reaction BENDICH and CHARGAFF (p 407) have extracted two antigenic fractions from *Proteus* OX19, one of which shows specificity with typhus sera and with *Proteus* antisera, the other with the latter only

The Pan-American Typhus Commission (p 703) have adopted as standard the Castañeda *Proteus* OX19 antigen

SIEVERS (p 890) uses living *Proteus* OX19 for the Weil-Felix test

A rapid slide test for typhus, in which serum and an emulsion of *Proteus* OX19 are used, is described by SANTO, readings are made within 12 minutes

For use in agglutination tests, SHEPARD and TOPPING (p 573) describe a method of preparing rickettsial suspensions from infected yolk sacs, which entails washing the rickettsiae, centrifugation, and absorption of much of the remaining yolk-sac material with Celte The method was satisfactory with the rickettsiae of epidemic and murine typhus, and Rocky Mountain fever, less so with Q fever and not at all with scrub typhus

GIROUD and JADIN (p 891) have used the rickettsia-agglutination test with epidemic and murine antigens, in epidemic typhus Homologous agglutination is at first no greater than heterologous, but becomes so at a later stage HAMMARSTRÖM *et al* (p 194) have found the rickettsia-agglutination test more sensitive and reliable than the Weil-Felix in typhus They describe the technique used, even the slightest microscopical clumping was regarded as positive In tests on refugees to Sweden from German concentration camps, in whom typhus occurred, HAMMARSTRÖM *et al* (p 652) found that the rickettsia agglutination test gave positive results about the 5th day of disease, but the Weil-Felix only about the 9th day The former, therefore, appears to be the more reliable in diagnosis

PACKALÉN (p 809) prefers the complement-fixation test to the rickettsia-agglutination test because of the difficulty of the Hammarström technique BERTSON (p 302) has shown that with the complement-fixation reaction, epidemic and endemic (murine) rickettsiae can be differentiated because the reaction with homologous strains is at a higher titre than reactions with heterologous strains She used 16 epidemic and 3 endemic strains in these tests, and the corresponding sera from convalescent guineapigs In comment, MEGAW points out that the margin of difference is not great MALCOMSON and WISHART (p 407) have been able to differentiate epidemic and murine typhus by means of the complement-fixation test in which type-specific antigens are used the titres being 2-4 times as high with homologous as with heterologous antigens The same authors (p 408) have written on the serology of typhus, but for details the original should be consulted

The quantitative complement-fixation test for typhus was used experimentally by VARLEY and WEEDON (p 654), who used various epidemic and murine antigens and guineapig antisera Although titres were high when homologous antigens and antisera were used there were some results which indicated that the test is not always type-specific in that one murine antiserum did not give high titres with all the murine antigens

GROUD and JUDS (p. 1057) have found that the complement fixation reaction is more sensitive than the Weil-Felix in giving positive results in persons inoculated with rabbit lung epidemic vaccine.

*Clinical findings—treatment.*—The clinical features observed in 244 cases of typhus in middle Europe during the war are recorded by LACHNITZ (p. 94). The incubation period was never less than 12 days. The liver was usually enlarged. An early leucopenia was followed by moderate leucocytosis. In many cases there were casts and red cells in the urine.

GROUD (p. 714) sets out the reasons why he thinks that inapparent and latent infections play a part in the epidemiology of typhus, and gives examples of the isolation of rickettsiae from apparently healthy persons. He regards the rickettsia-agglutination test as more reliable than the Weil-Felix. JUDS and BALMIST (p. 811) report two cases in which injection of gonococcus vaccine apparently lighted up latent typhus infections which had probably been present for some time. They suggest that such latent infection may play a part in the carry-over of infection from one epidemic to another.

HEIDER (p. 193) claims to have demonstrated rickettsiae in blood smears of patients with louse-borne typhus.

NORVITT (p. 633) states that electrocardiographic readings show abnormalities in most cases of typhus but thinks that extracardiac factors must play an important part in producing them.

VAN DEN ENDE *et al.* (p. 477) have written a substantial monograph on chemotherapeutic and other studies of typhus, in which they describe tests on 238 substances in animals, and trials in man of the two most favorable compounds. The results in man were not encouraging. The monograph also contains chapters on vaccine preparation (murine type in mouse lungs) and on the antigenic structure of epidemic and murine rickettsiae. These differ sufficiently to be regarded as distinct species but they contain antigens which are heat labile and which are not specific, as well as those which are specific.

HAAGV (p. 892) strongly believes that full doses of streptomycin, and of intravenous calcium given as early as possible are of great value in typhus.

MUGGAN *et al.* (p. 608) show that streptomycin has only slight inhibitory effect when administered into yolk sacs of embryo chicks shortly before inoculation with *R. prostratus*, less with *R. mooseri* and none with *R. vivax*. They think that it is unlikely to be useful in these rickettsial infections in man.

*Vaccination.*—PRINCEVICIUS *et al.* and RAJANEN (p. 653) have devised a new method of preparing the Weil vaccine, which is of feeding lice on a mixture of defibrinated blood and saturated bodies of infected lice through a membrane of skin from fresh human cadavers.

CURASSO (p. 809) having shown that guinea-pig blood is not toxic for human lice (as is generally thought) but that lice cannot digest it points out that they may be fed on guinea-pigs infected with *R. prostratus* and subsequently on immune human beings, and that they thus develop murine infection. This method of infecting lice has advantages over the Weil-rectal method. WRITZ (p. 1056) has found during the war in Poland that the louse intestine vaccine was much more effective than the mouse lung and yolk sac vaccines. He thinks that *R. prostratus* maintained in mice steadily approaches the murine type and that vaccines of murine type do not protect against louse typhus. MORINO (p. 1058) shows that in mice inoculated with the Weil vaccine the response to the rickettsia agglutination test and the protection afforded are according to the dose of vaccine given. STIEBER (p. 861) thinks that skin reactions to the Weil vaccine in persons who have previously received it are probably due to serum is to albumin from the bodies of the lice used.

The epidemic typhus in use of the U.S. Arm was very serious in preventing death, but the low incidence of the disease in Europe was due largely to M.L.

or DDT powders SADUSK (p 811) shows that the ether-treated yolk-sac vaccine of the Breinl strain given in 3 (later 2) doses at intervals of 7-10 days, with refresher doses every 6 months (later at the beginning and middle of the typhus season) protected against epidemic, but not against murine infection. GILLIAM (p 408) in Egypt showed that one or two doses of Cox vaccine had some effect in reducing the severity of typhus subsequently acquired, but little in prevention, three doses, however, did reduce the attack rate. BERKE (p 512) used the Cox vaccine with some success in Afghanistan.

GROUPE *et al* (p 197) describe the methods they used to increase the yield and potency of typhus vaccines prepared from infected yolk sacs, but for details the original should be consulted. BERKOWITZ (p 513) has increased the yield of yolk-sac cultures of epidemic and murine rickettsiae by inoculating with a small dose on the 7th day, which allows the embryo to live 11 days longer, when a good growth is obtained.

HAAGEN and CRODEL (p 196) describe a dried vaccine of yolk-sac cultures of murine and epidemic rickettsiae which, although not suitable for general use, had anti-infectious properties when tested in man (in Germany during the war), in that it apparently was effective against subsequent attempts at virulent infection.

FAJERSTEIN and BESDENJESZNICH (p 409) found that vaccination with 3 doses gave definite though not complete protection against typhus in Russian railway workers, and that after the course had been repeated in successive years the rate of protection increased.

SADUSK and KUHLENBECK (p 196) refer to an outbreak of illness after the use of live bile-attenuated typhus vaccine in Japan, and emphasize the risks of such a vaccine. In comment, however, MEGAW remarks on the good results achieved in French North Africa with this kind of vaccine.

FLECK (p 1057) has obtained from the urine of patients with typhus, a substance which, when injected into guineapigs, protects against the disease and produces positive reactions to the Weil-Felix reaction. He used this substance as a vaccine in man during the German occupation of Poland.

*Control*—SOPER *et al* (p 892) describe the use of louse powders (MYL and DDT) in the control of outbreaks of typhus in Italy during 1943-45. These outbreaks have been referred to several times in this *Bulletin*, but the present authors give much detail of procedure, which should be sought in the original. GEAR and MURRAY (p 702) state that outbreaks of louse typhus occur almost every year in the Africans of the Eastern Transvaal, but whereas control was formerly difficult, the use of DDT is now likely to eradicate the disease. A rapid slide test has been found useful in detecting the nature of an outbreak. MUSGRAVE (p 58) tested the lethal capacity to lice of garments impregnated with DDT in various proportions. Shirts holding 0.2 per cent of their weight of DDT were effective, the DDT persists at high temperatures and the chief loss of insecticidal power is due to loss of impregnated fibres from the surface of the cloth.

### *Flea typhus*

*Epidemiology*—MOOSER (p 191) has reviewed the research work of 20 years on the relationship between murine and classical typhus.

POLLARD *et al* (p 574) gave, by mouth, large doses of a saline suspension of yolk-sac material infected with murine typhus, to 6 healthy volunteers, of whom one became ill with a typical attack. They think that consumption of food contaminated by infected flea faeces, or rat urine, may be the cause of some cases of this disease, but in comment MEGAW suggests that in view of the large dose given in the experiment, the occurrence of this form of infection in nature is probably rare.

CODELLONCHI (p. 302) claims to have isolated a murine strain of rickettsiae for the first time in Ethiopia. By subinoculation in lice and guinea-pigs the strain showed a tendency to develop characteristics of the epidemic type.

KARXU (p. 893) states that it is now well known that human typhus in Shanghai is of murine origin. He performed the Weil-Felix reaction on the sera of rats for several years, and the percentage positive (1 in 100) fell from 10.3 in 1942 to 2.3 in 1945. There was a comparable fall in the number of positive reactions in human sera. In a fuller version of the same paper (p. 1059) he makes the point he has often stressed, that murine rickettsiae can adapt themselves, under exceptional circumstances, to transmission by human lice. Louse-borne epidemics in Shanghai tend to become arrested in hot weather. LIU (p. 574) found rickettsiae in fleas from rats trapped in a poorhouse in Persia, during an outbreak of typhus. A large proportion of the rats (*R. norvegicus*) showed positive Weil-Felix reaction. He also isolated rickettsiae from the mite *Liponyssus bacoti* found on the rats, but he thinks that fleas are the chief if not the only vectors.

WILEY (p. 199) thinks that typhus of murine origin is much more prevalent in the United States than the reported figures indicate. In the north it is found only in business areas of towns, but in the south cases also occur in rural districts. For control DDT, calcium cyanide, sodium fluoroacetate and AITL are all useful. The incidence rate of flea-borne typhus in part of Alabama was 4.28 per 100,000 in 1943, and HILL and LACRAVUS (p. 891) show that it was about the same in rural as in urban localities, infection being obviously associated with dusty work in rat-infested places. BECK *et al.* (p. 885) discuss the incidence of typhus of murine type in California since 1916.

RITZ-SANCHEZ *et al.* (p. 304) found positive Weil-Felix tests in 16 per cent of apparently healthy persons in part of Mexico, where murine typhus is common.

POWERS LEBRON *et al.* (p. 196) found positive complement-fixation reaction (with an epidemic type antigen) in about half the rats trapped in Porto Rico, but the Weil-Felix reaction was positive in only a small proportion. Typhus of murine origin is common in the area.

TESTS.—Using the Fitzpatrick slide technique (this Bulletin 1945 v. 4, 382) NELSON (p. 703) has found the rickettsia-agglutination test (also) for differentiating murine from epidemic typhus and Rocky Mountain fever. Results not always obtained with other techniques. This test was more specific than the Weil-Felix and became positive earlier than the complement-fixation reaction in the 22 cases of murine typhus tested.

POLLARD *et al.* (p. 303) have devised a test in which the lances of fleas infected with murine typhus are used for complement fixation with homologous immune sera. This provides a rapid method of detecting the infection in the flea.

TREATMENT.—DÍAZ RIVERA *et al.* (p. 109) report decided benefit from *p*-aminobenzoic acid in the treatment of a few cases of murine typhus. Methylene blue, either by subcutaneous injection or by the mouth, was found useful in the treatment of mice infected with *R. mooseri* and HIKETA and SCHILLING (p. 104) think that it is worth trial in man.

VACCINATION. Control etc.—OZ (p. 59) describes the method of preparation of murine vaccine carried out at the Hadassah Institution, Jerusalem.

Fleas and other ectoparasites of rats can be well controlled by using DDT (10 per cent powder) in their burrows, but complete elimination is not achieved (LEWIS and NICHOLSON, p. 574). On the other hand if DDT is thoroughly and carefully applied to the haunts of rats the number of fleas can be reduced almost to zero. DAVIS (p. 705) reaches this conclusion as a result of work on murine typhus control in Texas. In an account of measures taken in part of Texas to control typhus of murine origin COOPE (p. 180) shows that by dusting rat runs with DDT reduction in the incidence was achieved, and that good



results were obtained against the rats themselves by the use of sodium fluoroacetate. The significance of the complement-fixation test in rats is thought to be doubtful. Instructions for the destruction of rats and their fleas, as a measure of control of murine typhus and plague, are given by ELISHWITZ (p 1064), who uses DDT and the rat poisons ANIU and sodium fluoroacetate.

*Proctus OXK type vector mite*

*Epidemiology transmission*—KALRA (p 575) quotes figures which indicate that mite, flea and tick typhus are widely distributed in India, and that the mite-borne disease is especially prevalent in Bengal, Assam and Madras. *R. orientalis* has been recovered from *Trombicula deliensis* mites which are abundant at 7,000 feet in the Kumaon Hills. ADY (p 577) noted that the differences observed in various parts of Assam in the risk of infection of troops with scrub typhus were correlated with the presence or absence of *T. deliensis*. These mites could be taken to indicate the movements of rats and by trapping rats an impression of the presence of mites could be obtained.

BRUNEAU and NGUYEN-DINH-DIEP (p 655) report an outbreak of scrub typhus in a garrison of a fort in Indo China. All the 16 cases occurred in the 139 Annamite soldiers; none in the 90 Thais, the freedom of the latter may have been the result of immunity due to previous contact with the infection. A few cases of scrub typhus were reported in American troops in China but it is not known how widespread the disease is. MILLSAUGH and FULLER (p 705) have found *Trombicula deliensis* on various mammals and birds in Yunnan and Kweichow provinces and this appears to be the first record of this mite from China.

PHILIP (p 989) studied scrub typhus in part of Japan where it has been endemic for many years, but where the incidence is falling. Complement-fixation tests with different strains of *R. orientalis* gave very diverse results with the same sera, a point to bear in mind. He (p 990) has written on the identification of the mites of voles in Japan.

In Dutch New Guinea GRIFFITHS (p 1060) studied rats and their mites in various locations. There was no evidence that the rats (*R. concolor* group) were infected with scrub typhus in the rain forest, but abandoned village and garden areas, and beach and forest margins were definitely associated with transmission of the disease. *Trombicula deliensis* was the common mite.

PHILIP and WOODWARD (p 305) report their observations on the *Trombiculid* mites of the Philippines.

JOHNSON (p 200) states that there is strong evidence that *Rattus praecox* played a part in the epidemiology of scrub typhus in the Solomon Islands during the war.

*Aetiology*—GIROUD (p 304) has studied the relationship between morphological appearance and pathogenic properties of two strains of scrub typhus rickettsiae.

SMADAL *et al* (p 513) have found a toxin lethal to mice in yolk-sac cultures of the Gilliam strain of *R. orientalis*, which can be neutralized by highly diluted homologous antisera. Certain other strains did not produce a toxin.

DIERCKS and TIBBS (p 894) found that the best results for staining *R. orientalis* are given by MacNeal's tetrachrome stain, they give details for its use.

*Pathology*—In a study of the pathology of scrub typhus LEVINE (p 59) shows that the changes are quite similar to those found in epidemic typhus—haemorrhages, perivascular exudation, consolidation of the lower lobes of the lungs. Oedema of the ankles, or collection of fluid in serous cavities, is common. It seems likely that patients who recover show no residual cardiac damage.

TULLIS *et al* (p 895), as a result of examining mice, monkeys and one man infected with the Karp strain of *R. orientalis*, are inclined to think that in

scrub typhus, damage to the endothelium of the vessels is much less severe than in Rocky Mountain fever and epidemic typhus but MAGAW demurs at this, pointing out that different strains of infecting organisms produce lesions of different severity and quoting other authors who have not found essential pathological differences between the diseases.

WELL and HAYMAKER (p. 577) report on the pathology of the nervous system in scrub typhus. The chief changes found in 21 fatal cases were engorgement of the vessels of the leptomeninges and cerebrum sometimes with marked cellular infiltration. Focal nodules were few.

Tests.—In a series of patients with scrub typhus, from Burma and the Philippines, whose sera were examined at various stages by the complement fixation reaction in which three strains of rickettsiae were used, HAYMAKER (p. 60) found remarkable variations in response. There is, however, no clear differentiation of serological types. Higher and more persistent titres were obtained with this than with the Weil-Felix test. The same author (p. 61) describes the preparation of an antigen from a strain of scrub typhus rickettsiae from Malaya. The organism was grown in yolk sac culture and the antigen was specific for scrub typhus giving negative results with other diseases, including those of the typhus group. SHE (p. 304) describes how the complement fixing antigen is separated from suspensions of scrub typhus rickettsiae.

BELL *et al.* (p. 514) have noted antigenic differences in three strains of *R. orientalis* as measured by cross-neutralizing tests.

Clinical and treatment.—SAYEN *et al.* (p. 305) report on 200 cases of scrub typhus in American soldiers in Assam and Burma. It was not possible in the first week of illness to tell if the attack would be mild or severe. There was a primary lesion in 60 per cent and this with lymphadenopathy, rash, engorgement of retinal veins or oedema of the retina and Weil-Felix (OXA) 1 in 100 or more was a useful diagnostic sign. Some degree of pulmonary involvement was usually present as was albuminuria. The nervous system was involved in a minority of cases, and haemorrhages were common in several cases. Complications, hyperpyrexia, restlessness, tachycardia and cyanosis were ominous signs; the case mortality rate was 8.5 per cent though in other series it was lower than this.

RIPLEY (p. 200) notes that in one outbreak of scrub typhus in the Pacific all patients showed some involvement of the central nervous system from transient toxic cerebral symptoms to evidence of widespread inflammation with coma and death. The pathological lesions found were similar to those seen elsewhere in the body, focal lesions with necrosis, thrombosis and perivascular infiltration. Many of the patients showed residual manifestations which seemed to be secondary to the changes in the nervous system but psychotherapy was of some value.

TESSLERTON (p. 806) describes 58 cases of scrub typhus and 4 of urban typhus in troops near Kuala Lumpur. The latter could be differentiated from scrub typhus without doubt only by the results of the Weil-Felix test and by its fatal outcome.

M. LIMANS and GRANT (p. 46) show that methylene blue given with food in a concentration of 0.2 per cent is triply effective in reducing fatality from scrub typhus in Swiss mice especially when combined with administration of oxygen even when started as late as 140 hours after inoculation. Para-aminobenzoic acid was less effective. PETERSON and FOX (p. 613) report that if methylene blue or toluidine blue is given in food to mice infected with the hard strain of *T. muris* as late as 48 hours after the onset there is a substantial therapeutic effect. The corresponding dose could not be tolerated by human beings and intramuscular injection is adequate for calves.

haemolytic anaemia Nevertheless, the results are encouraging, especially when *p*-aminobenzoic acid is given at the same time

**Vaccination**—LEWTHWAITE *et al* (p 410) describe the techniques they adopted in cultivating *R tsutsugamushi* (*R orientalis*) in the yolk sacs of hens' eggs, for the purpose of preparing vaccines Details should be sought in the original Antigens suitable for complement-fixation and rickettsia-agglutination tests could not be obtained in this way [It will be remembered that vaccine for scrub typhus was eventually obtained from infected lungs of cotton rats] HENDERSON-BEGG and FULTON (p 577) standardized the scrub typhus vaccine prepared from lungs of cotton rats by a simple technique for counting the rickettsiae WALKER (W T) (p 706) shows that scrub-typhus vaccine prepared in England was effective in reducing the severity of attacks of the disease, in 16 cases, even if only one dose had been given On the other hand, CARD and WALKER (J M) (p 707) could find no satisfactory evidence that the attacks were favourably influenced in 33 men in S-E Asia Not all had received the full course

*Indeterminate type vector tick*

STEINITZ (p 307) reports, for the first time, a case of boutonneuse fever in Palestine

BENGTSON (p 812) discusses nomenclature of the rickettsiae of Rocky Mountain fever and of murine typhus, readers should consult the original for details

HUMPHREYS and CAMPBELL (p 758) have found evidence of infection with Rocky Mountain spotted fever in collections of *Dermacentor andersoni* made in British Columbia and Alberta They make the point that failure to recover *R rickettsi* from ticks should not be relied upon as an indication that an area is free from infection, there may be strains which are mild for guinea-pigs but virulent for man BUSTAMANTE and VARELA (p 656) found *Amblyomma cagayense* naturally infected with Rocky Mountain spotted fever in Veracruz, Mexico

VALLEJO-FREIRE (p 708) shows that the rickettsia of tick-borne typhus of Mexico is apparently identical with that of Rocky Mountain spotted fever of North America and of Brazil He proposes the name spotted fever for this disease, but in comment MEGAW shows that this name, which has been applied to other diseases, is less suitable than tick-typhus

Discussing the Weil-Felix reaction in Rocky Mountain spotted fever, PLORZ (p 201) stated that the usual reaction is of the *Proteus OX19* type, but that the *OX2* titre is sometimes high, and that if it is 1 in 320 or more the disease can be suspected. In comment MEGAW draws somewhat different conclusions from the data given, and thinks that either the *OX19* or the *OX2* titre may vary from 0 to +++++

DE PAULA (p 201) describes vesicles on the palate and white ulcers on the fauces, in cases of typhus [presumably tick-borne] in Minas Gerais

FLINN *et al* (p 413) report good results from *p*-aminobenzoic acid in human cases of Rocky Mountain spotted fever It is rapidly excreted in the urine and repeated administration is therefore necessary The authors gave 4-6 tablets (each of 0.5 gm) every 2 hours, to a total dosage of 50.4-327 gm RAVENEL (p 708) writes very favourably on the effect of *p*-aminobenzoic acid in Rocky Mountain spotted fever, as a result of its use in 5 cases ANIGSTEIN and WHITNEY (p 412) think that administration of calcium gluconate together with *p*-aminobenzoic acid increases the value of the latter in experimental Rocky Mountain spotted fever in guinea-pigs

Complement-fixation reactions were carried out on the sera of 40 patients (in India) whose Weil-Felix reactions were of the *OX19* or *OX2* type, by

SEATON and STOKER (p. 578) who used murine and Rocky Mountain spotted fever antigens. Of 18 positive for murine typhus the Weil-Felix was of OX19 type in 14 of 18 positive for Rocky Mountain fever 12 gave the OX<sup>19</sup> type of reaction. Controls were negative. The authors therefore regard this as further evidence of the presence of tick typhus in India. HALRA (p. 575) has isolated strains of rickettsiae (one from a patient in Poona and one from *Haemaphysalis leachi* var. *indica* in Imphal) which show some antigenic relationship to *R. rickettsii*.

PRONIKHINSKI (p. 898) describes the tick typhus of the Soviet Far East which is probably transmitted by *Dermacentor glauco* and *Haemaphysalis concinna*. PETRIJARI (p. 515) in Soviet Asia describes a disease which he claims is tick borne and in which after a febrile period of 8-10 days, the Weil-Felix reaction with *Proteus* OX19 becomes strongly positive.

A small outbreak of tick typhus was reported by ASHRAW *et al.* (p. 202) from Queensland, Australia. There was an eschar with associated lymphadenitis in most of the cases and in two an adult tick was found at the site of the lesion. It seems likely that *Ixodes holocyclus* is the tick concerned, but others occur in the area. The Weil-Felix reaction gave results somewhat like those reported in Rocky Mountain fever but complement fixation tests on the sera of the patients failed to show any immunological relationship with that fever or with S. African tick bite fever boutonneuse fever epidemic or murine typhus. The rickettsiae were cultivated by PLOTS *et al.* (p. 204) and the sera of animals infected with them reacted to the homologous antigen but not to the antigens of other fevers of the typhus group including Q fever (though there was some rather indefinite evidence of immunity to S. African tick bite fever and murine typhus which may have been non-specific). The rickettsiae is probably a hitherto undescribed species. FURTHER and JACKSON (p. 204) report their laboratory comparison of these tick typhus rickettsiae with murine strains: there was some incomplete cross immunity. FENNER (p. 514) found low titre positive complement fixation reactions with the sera of opossums bandicoots etc tested with an antigen from a rickettsiae of North Queensland tick typhus. The animals were from an area in which the disease had been reported.

### Q fever

In 1945 a disease which occurred in British and American troops in Italy and which had previously been found in Greece was shown to be Q fever. The diagnosis made before this identification was atypical pneumonia and Balkan grippé. Q fever had not hitherto been seen outside Australia and the United States. Various papers in the *American Journal of Hygiene* describe the steps of its identification made—

ROBIN and RAGAN (p. 67) show that the onset was sudden with fever and cough. Signs of patchy consolidation of the lungs appeared, verified by X-ray. There were no deaths. Blood cultures were sterile the Weil-Felix test negative but *Rickettsia burnetii* was isolated 16 times in 21 attempts by inoculation of guinea-pigs. Sulphonamides and penicillin were useless.

In five of the outbreak the possible modes of infection were studied and ROBIN, GUILD and WALKER (p. 63) noted that the men affected in one unit were those who had slept in or entered the loft of a barn in which pigeons, cats, larval ticks, fleas and mites were found. They think that as few of the men complained of bites an insect vector was unlikely but inhalation of dust containing dried secretions of animals may have been a factor. The possibility of person-to-person transmission.

The rickettsiae were isolated from 16 patients through guinea-pigs through readily in both cases of chick embryos. HARRIS, RICHARDS and WALKER (p. 64) show that different strains from Italy and America, gave

different results with the complement-fixation test on sera from human cases and from guinea-pigs, these differences are probably quantitative, and they were not apparent in the rickettsia-agglutination test

ROBBINS and RUSTIGIAN (p 65) think that in the laboratory outbreak which occurred in Italy, the infection was probably acquired by inhalation of air infected usually in the process of yolk-sac culture work

FEINSTEIN *et al* (p 66) describe the symptoms and signs of 143 men whose attack of Q fever began in the United States after a voyage of 9 days from Naples. In most of them there were middle- and lower-zone pulmonary lesions visible on X-ray, which differed in distribution and character from those of primary atypical pneumonia. Similar signs were seen in some men who had no symptoms. Diagnosis was confirmed serologically.

The U.S. Commission on Acute Respiratory Diseases (p 67) could find no explanation of this outbreak, which involved other units which had been at the same camp in Italy. They think that an arthropod vector may have been involved, while the men were cleaning the camp before leaving it, and were sleeping in the open. The causal organism was not isolated, but complement-fixation tests were usually positive in rising titre. Some positive results were found in another unit which had apparently escaped infection. The Commission (p 68) gives details of the identification and characteristics of a strain of Balkan grippé rickettsiae isolated in guinea-pigs in Greece. Sera of guinea-pigs inoculated with this strain, and of human patients, gave positive complement-fixation tests with antigens from Australian or Italian *R. burneti*, and rickettsia-agglutination tests on sera of guinea-pigs or patients gave similar results with this and the Australian and Italian antigens.

The Commission (p 69) recounts the history of the laboratory infection referred to above; rickettsiae were isolated from the blood of some patients and the pleural fluid of one. Symptoms were severe, but the infecting dose (presumably inhaled during manipulation of infected yolk sac material) may have been heavy.

CHENEY and GEIB (p 70), having seen cases of atypical pneumonia in Panama, inoculated guinea-pigs with the blood of some of the patients, and found that one of them was a case of Q fever, of which the rickettsiae showed cross-immunity with the standard American strain. The patient had been in the area for 3 months; no indication of the mode of transmission was found.

TOPPING *et al* (p 70) show that 6 strains of Q fever rickettsiae from widely different sources grew readily in yolk sac cultures and were similar in morphology. Five of them showed complete cross-immunity (the sixth could not be tested) but the various antigens were not equally sensitive in the complement-fixation test.

BLANC *et al* (p 709) isolated three strains of *R. burneti* from *Hyalomma savignyi* (? *H. aegyptium*) in southern Morocco. BLANC *et al* (p 898) give reasons for their view that the gerbil *Meriones shawi* is a host of Q fever in Morocco, where *Hyalomma savignyi* is the vector.

HUEBNER (p 709) describes an outbreak of Q fever at the National Institute of Health, Bethesda, U.S.A., where 6 strains were being investigated. The outbreak was closely associated with preparation of yolk-sac antigen, involving high-speed centrifugation and treatment with 0.5 per cent formalin, which has not been found lethal to this rickettsia. In comment, Megaw remarks that it is difficult to reconcile the findings with any other hypothesis than the inhalation of droplets of infected yolk-sac material. Persons who had suffered from the disease during an outbreak in 1940 were not this time affected, and persons who had received Rocky Mountain fever vaccine were apparently protected to some extent, but not completely; typhus vaccination did not confer any protection. The incubation period was 13-18 days.

TOPPING and his colleagues (p. 710) describe an outbreak of Q fever in stock handlers and slaughterhouse workers in Texas who were probably infected by dust derived from material contaminated by the excreta of a group of apparently healthy cattle. There was no evidence of transmission by ticks. Autopsies usually revealed lesions similar to those of atypical pneumonia. In complement fixation tests with Q fever antigens, rising titres were found to 1 in 320 in 4-5 weeks. *R. burnetii* was isolated from two patients through mice, and yolk sac cultures were readily obtained.

### *Rickettsialpox and other diseases*

The newly recognized rickettsialpox is described by HILGNER *et al.* (p. 411) from New York, where an outbreak of 80 cases took place. The clinical features resemble those of chickenpox, but rickettsiae were isolated through mice from one of 15 patients. There is apparently some degree of cross immunity between this disease and Rocky Mountain spotted fever.

GREENBERG *et al.* (p. 707) describe rickettsialpox. Almost all patients showed a primary lesion—a papule which became a vesicle and then a scar. The onset of fever was sudden and the fever was remittent, ending by lysis in 1-10 days. A rash was present in all cases, lasting 4-7 days, and becoming macular. Positive complement fixation tests were given with an antigen prepared from rickettsiae from one patient but this antigen did not react with sera from patients with certain other rickettsial diseases, though it did with sera from Rocky Mountain spotted fever.

GREENBERG *et al.* (p. 694) give details of the epidemiology of rickettsialpox. Mites (*Urodeum yasuii sanguisuga*) were found on the walls of incubators and on mice and the authors point out that if incubators are irregularly used they conduce to mouse infestation. HILGNER, JELSON and LOVINSKY (p. 411) isolated two strains of the rickettsia of this disease (*R. akari*) from mice (*Urodeum yasuii sanguisuga*) collected from mice and from the walls of incubators in the areas concerned. Other strains were also isolated from pools of mites, but could not be cultivated in fertile eggs. One of the mice was attacked by the disease three weeks after collection; the mites HILGNER *et al.* (p. 697) have recovered *R. akari* from naturally infected mice at the end of the outbreak of rickettsialpox and have identified them by various tests. The mice appear to be the natural reservoirs of the disease.

In an interesting paper BURKE (p. 206) describes a hitherto unrecorded species of rickettsia which gives an inapparent infection in voles and is found in the St. Lawrence River, Canada. This is immunologically closely akin to the harp strain of *A. orientalis* and is probably transmitted by mites (*Urodeum yasuii sanguisuga*) found on the voles and from which rickettsiae were recovered.

A laboratory outbreak of trench fever in persons employed in feeding large numbers of lice for the preparation of *W. 41* vaccine is described by CODELLONATI (p. 307) from Adria, Italy. Lice thought to be clean were found to be harbouring rickettsiae which were apparently identical with *R. quintana*. The symptoms were typical trench fever. BURKE (p. 1081) and SCHULZ and KATZ (p. 1161) give their reasons for thinking that one form of field nephritis seen during the war may have been due to *Rickettsia* in urine.

NEJEDLI (p. 46) claims to have cultivated rickettsiae in the absence of living cells. With DOUGLAS (p. 57) he describes rickettsial leucocytes. The Congo human that the finding of rickettsiae in the urinary sediment is one of the best methods of diagnosis. He (p. 57) shows that the mouse protection test for yellow fever remains valid for patients with Congo typhus. He has noticed (p. 5) that healthy laborers can cause just harbour rickettsiae.

indistinguishable from those which he has cultivated from the blood of typhus patients, but this latent rickettsial infection does not interfere with the use of the animals for typhus work

BARLOVATZ (p 810) describes an attack of a typhus-like fever, with Weil-Felix reaction (*Proteus OX19*) positive to 1 in 640, which he himself had some 3 months after leaving the Belgian Congo. He suspects that it was the Congo form of typhus with prolonged incubation period. *Charles Wilcocks*

## RABIES

VEERARAGHAVAN, N. Further Observations on the Cultivation of Rabies Virus *in vitro* *Indian J Med Res* 1947, Oct, v 35, No 4, 237-53 [12 refs]

The author has previously claimed [see this *Bulletin*, 1947, v 44, 635] that the aetiological agent of rabies can be cultivated *in vitro* in a medium consisting of sheep brain extract with various additions, and that for this reason it may not be a true virus. In a continuation of this work it is stated that the addition of tryptophane, thiamin, pyridoxine and pantothenate increased the amount of virus obtained in cultures. The maximum titres observed were  $5 \times 10^9$  LD<sub>50</sub> per cc, which were obtained 24 hours after adding virus to the culture medium at a concentration of  $5 \times 10^5$  LD<sub>50</sub> per cc. Propagation of virus in culture was observed through 4 passages.

[This latter fact, together with the high titres reported in this paper, certainly supports the author's claim that true multiplication is occurring, as opposed to an apparent rise of titre caused by dispersion of virus aggregates or the breakdown of combinations with inhibitory substances. Independent confirmation will be awaited with interest.] *D J Bauer*

## MALARIA

J. NATIONAL MALARIA SOC 1948 June v 7 No 2 148-56. Medical Research in Malaria 1947. Report of the Committee on Medical Research [HAAS V H, Chairman]

NOYAN, A. Summary of the Free Lecture on Malaria. *Acta Med Turcica* Ankara 1948, v 1, No 1, 32-7, 2 folding maps

This summary of a lecture which was given at the Ankara Numune Hastanesi in May 1946 is semi-popular, but gives some useful information on the distribution and control of malaria in Turkey.

The malarial regions of the country are shown in a shaded map, prepared by the author for the first Turkish Medical Congress in 1925. This indicates the "first malarial region" which includes districts having average parasite and spleen indices of 25 per cent or more, and comprises the coastal regions, great river beds and the south-eastern part of the country. The "second malarial region" includes the mountains and high plateaux where the disease is usually introduced from the first malarial region, but where it is not ordinarily prevalent. An anti-malaria campaign has been in action since 1924, and although it was somewhat relaxed during the war, it has been intensified in the last two years with good results. In the army, for example, where statistics are readily available, cases of malaria have fallen by half.

The common anophelines are *A. maculipennis*, *A. sachsi*, *A. superpallens*. In South Turkey and near Palestine *A. levyeri* and *A. sergenti* are encountered.

Epidemiological conditions are favourable to malaria along the Black Sea and Mediterranean coasts, the river beds, in South-East Turkey and in those parts of Anatolia below 1,000 metres.

In the warmer regions along the Mediterranean coast malaria may begin in April-May and last until October-November. Benign tertian malaria is relatively common but in some districts the subtertian form is more frequent. Quartan malaria is less common. Cases reported to the first Medical Congress from various hospitals amounted to 9,971 and comprised 5,438 benign tertian, 4,140 subtertian and only 395 quartan infections.

Malignant forms of the disease are not met with as commonly as they are in the tropics and they are not usually fatal. In the first world war the Turkish Army recorded 400,000 cases of malaria with a mortality of 4.8 per cent. In 1944-45 the death rate was as low as 0.4 to 0.33 per cent.

Control presents difficult problems: the malarious districts are the richest and most fertile and attract thousands of workers yearly from the less fertile Anatolia; the crop time coincides with the malaria season and the workers sleep out of doors, often on flat roofs or in gardens. Some of the houses have thatched roofs which harbour mosquitoes and pools are maintained in some villages to provide water for buffaloes and ducks.

Drug prophylaxis with various formulations of quinine and of atabrine (mepacrine) has been employed and the various methods compared but comparable results were not available at the time when the paper was published.

H. J. O'D. Burke Gaffney

SAUTET J., RAYMON, J., VILLERT F. & VILLERT J. Quelques notes parasitologiques sur le paludisme et l'anophélisme en Mauritanie. (Some Parasitological Notes on Malaria and Anophelines in Mauritania.) *Méd. Trop. Marseille*, 1948, Jan. Feb., v 8, No. 1 32-9 1 map

In a rapid and incomplete survey of parts of Mauritania (French W. Africa) the following anophelines were found: *Anopheles gambiae*, *A. fuscus*, *A. pharoscus* and *A. rufipes*. The dates of capture in some half-dozen localities are given. Adults were taken in houses and their buildings and larvae in both temporary and permanent waters. Of 307 blood slides examined 180 were positive as follows: *Plasmodium falciparum* 133 (52 from children under 15 years of age), *P. malariae* 33 (8 children under 15), *P. tritax* 14 (5 children under 15). Of gametocyte carriers, 4 had *P. malariae* and 22 *P. falciparum* and *P. tritax*. The authors draw attention to the predominance of *P. falciparum* infections, the rarity of *P. malariae* and the still greater rarity of *P. tritax* but they admit that owing to the small numbers examined they are unable to draw any conclusions.

H. S. Lewis

MCDONNELL, G. E. & HENDRICKS, F. M. *Plasmodium malariae* in School Surveys in South Carolina. *J. National Malaria Soc.* 1948 Mar. v 7, No. 1 65-75 2 maps (11 refs.)

Between 1937 and 1943 the South Carolina State Board of Health carried out thick film blood smear surveys among school children in 23 counties. Altogether 108,559 smears were collected from 560 schools for white children and from 918 schools for coloured children. Of this total 10,287 were from 13 schools for white children and 77 schools for coloured children in which the 295 positive *P. malariae* blood films were found. The percentage positive



*P. malariae* films for white children were 0.64 and for coloured children 3.23 thus *P. malariae* infection is primarily an infection of the coloured race in this State

One or more schools in 15 counties gave positive *P. malariae* smears, in only 8 of these counties were white children found infected. The counties with most *P. malariae* infection were Calhoun, Berkeley, Dorchester, Orangeburg, Sumter, Georgetown and Clarendon. Infection is concentrated along the course of the upper Santee River. *P. malariae* was found most frequently in smears taken in December. Norman White

VUILLET, J. & LEVAVASSEUR, G. Excitation biologique des ultra-sons sur des oeufs d'*Anopheles maculipennis* [Biological Stimulation of *Anopheles maculipennis* Eggs by Supersonic Rays] *Méd Trop* Marseille 1947, July-Oct, v 7, No 4, 343-6, 3 charts

Eggs of *Anopheles maculipennis* were exposed to supersonic radiation produced by powers ranging from 250 milliamps to 1,200 milliamps. The periods of exposure varied from 15 seconds to 15 minutes. In some experiments the radiations were concentrated by a concave mirror and in others reflected from a convex surface. The rate of development of the larvae hatching from these eggs was studied and compared with that of larvae from normal untreated eggs. It was found that the rate of development was accelerated in those larvae from eggs which had received radiations at powers above 1,050 milliamps and concentrated by the concave mirror. For instance, larvae were still in the first instar and only reached the third stage after nineteen days. In a few trials done with a convex mirror, no acceleration of larval development was observed. Other trials indicated that, varying the period of exposure, within the experimental limits, at any one power made little difference, and in July when the mean temperature of the water was 26°C, larvae from treated eggs were still more advanced than those from normal eggs, just as in May when the average water temperature was only 20°C.

In discussing this phenomenon, the authors discard the effect of heat as a cause because with an exposure of 15 seconds they say the water had no time to warm up, but the reviewer cannot help feeling that there may be a local transitory thermal stimulus which they have overlooked. It appears that only a few eggs can withstand the radiations and remain floating, these hatch but the majority burst and sink, thus showing that such treatment is very near the threshold of destruction. H S Leeson

COUTINHO, J. de O. Contribuição para o conhecimento das espécies do subgênero *Kerteszia* (Diptera Culicidae). Sua importância na transmissão da malária. [Observations on the Sub-genus *Kerteszia* and its Importance in the Transmission of Malaria] [Thesis for Doctor's Degree] Universidade de São Paulo, Faculdade de Medicina 1946. 87 pp. 2 maps, 2 text figs and 12 figs on 3 pls [Bibliography] English summary

DULANEY, Anna D. with the technical assistance of Jane B. Priest, Mary L. Almeda & B. Parker. The Complement Content of Human Sera with especial reference to Malaria. *J Clin Investigation* 1948, May, v 27, No 3, Pt 1, 320-26, 6 figs [18 refs]

With the use of a modification of the method of Kent, Bukantz & Rein [see *Journal of Hygiene*, 1946, v 21, 775] the amount of complement in the blood

of (1) 30 normal individuals, (2) 23 persons with liver disease, (3) 32 persons with non-infectious diseases and (4) 23 neurosyphilitics before and after induced malaria (presumably P. at though this is not stated) was determined.

The authors reach the following conclusions —

1. The over-all complement content of normal human sera (as based on the amount in milliliters required for 50 per cent. hemolysis) is remarkably constant.

2. The 50 per cent hemolytic unit for normal individuals, as determined by the method employed by us, ranged from 0.0032 to 0.006 ml. with a median of 0.0045 ml.

3. Day-to-day variations in the complement content of normal individuals appear to be slight.

4. The complement level of sera (one sample) from patients with liver disease and from patients with non-infectious diseases of various types did not appear to be depressed. There was no correlation between complement titer and the results of the cephalin-cholesterol test.

5. Complement is usually diminished during the course of induced malaria. This decrease may be very slight or in severe disease it may be very marked. In general the complement titer reflects the severity of the disease, the balance between host and parasite. Complement titer cannot be correlated with parasite count, white blood cell count, temperature, number of paroxysms, hours of fever, cephalin flocculation test or antibody titer.

6. In any study of complement as related to a particular disease it is important that a series of determination be carried out at short intervals during the course of the disease in order to detect changes which may occur.

(R. D. Lewis)

DI LIZIO C. Malaria before and after. (Diagn. & differential clinical. Clinical Differential Diagnosis of Malaria and Relapsing Fever). Bull. Soc. Ital. di Mal. Trop. 7 (Ser. I) 1947. 7 Nov. 54 416—English summary (2 lines)

SAKOLY C. PROST & CAMERON L. A malignant form of malaria. Bull. Soc. Med. Trop. Ind. 1947. 7 Nov. 7/8 115-17 fig.

RAT L. Malarial Diabetes. Report of a Case. Lancet 1948 July 3 111 fig.

A man of 43 returned from India in June 1947 after six years' residence there. A few weeks later he suffered from frequency, nocturia, excessive thirst and loss of weight. He had had malaria at the age of 19. There was no significant family history.

On examination on August 21st, glycosuria was present but no acetone bodies were found. Ring forms of *Plasmodium falciparum* were found in the blood.

Next day the patient's fasting blood sugar was 350 mgm/100 cc. Two days later he became worse, he felt drowsy and could not walk unaided. The fasting blood sugar was unchanged but the glycosuria was heavy and acetone bodies were present in the urine. He was given 30 units of insulin three daily and a diet of 2,500 calories. Next day his fasting blood sugar had dropped to 182 mgm/100 cc. For two weeks the patient improved, the glycosuria disappeared, but the fasting blood sugar was still raised. On September 17th,

when insulin had been reduced to 30 units twice daily, leading to the reappearance of glycosuria, Paludrine was given in a dosage of 0.1 gm twice daily for 10 days. The urine then became sugar-free, although the diet was unchanged and the insulin dosage was 30 units a day. By October 9th, the fasting blood-sugar was 104 mgm/100 cc and by the 31st, the patient was no longer on a restricted diet nor was he receiving insulin.

Three months later, after consistently negative weekly examination of the urine for sugar, the result of a sugar tolerance test was within normal limits.

The author considers that the diabetes was caused by malaria affecting the islets of Langerhans. He refers to two cases of severe subtertian malaria, with sudden death, sections from which were shown to him by Professor R. J. V. Pulvertaft, in these, the capillaries of the islets of Langerhans were completely blocked by red blood corpuscles loaded with parasites (one of these sections is illustrated in the text).

It is presumed that a similar pathological process occurred in the present case, in which the diabetes could be controlled by diet and insulin, and was cured by Paludrine.

H. J. O'D. Burke-Gaffney

EYLES, D. E. & YOUNG, M. D. Studies on Imported Malaria. 7. The Parasitological Pattern of Relapsing *Plasmodium vivax* in Military Patients. *J. National Malaria Soc.* 1948, Mar., v, 7, No. 1, 23-37, 3 figs.

In their studies of relapsing *P. vivax* malaria acquired overseas, the authors examined the blood of their patients twice a week after the treatment of clinical attacks. In 77.2 per cent of relapse attacks in 351 patients under observation, parasites were found in the blood before fever occurred, this percentage would have been higher had daily blood examinations been practicable. On the average the first parasites were found 3.5 days before the febrile paroxysm. The median fever threshold parasite count for over 800 relapse attacks was 3,200 per cmm (mean 6,300). For Pacific cases these figures were 2,952 and 6,030, for Mediterranean cases 3,836 and 7,250. No significant variation in parasite level was found between early, middle and late relapses.

Pacific cases showed male gametocytes to be present in 29.4 per cent of 659 attacks against 55.7 per cent in the case of 185 Mediterranean attacks, a highly significant difference. Patients with or without gametocytes during one relapse were likely to be with or without, respectively, during the subsequent attack.

Delayed primary attacks, nearly all from the Pacific, occurred on the average 49.1 days after suppressive atabrin had been discontinued. Extreme intervals were 7 and 167 days. The median value of the first parasite count after onset of fever in delayed primary attacks was 870 per cmm for 197 cases. In 63 of these cases in which the onset of symptoms was reported promptly, the median value was 150 parasites per cmm.

The mean interval, without regard to the drug used, from the onset of one to the onset of the subsequent clinical attack was 61.1 days, most relapses had taken place by 120 days. Most patients had no demonstrable parasite activity between relapses but about 12 per cent had transient low-level asymptomatic parasitaemia 56 days (average) after the onset of the previous clinical attack and lasting 12 days (average), varying from one to 62 days.

Three hundred and fourteen patients were kept under observation for four months or longer after their last clinical attack. About 25 per cent of these showed terminal asymptomatic parasitaemia, about half of these persisted for more than a month. These parasitaemias were both remittent and intermittent. They were first observed about 80 days (average) after the last

observed clinical attack. Levels attained by these parasitaemias were usually only one fourth to one half the levels noted in the same patients at the time of the previous clinical attack.

Malaria parasites were present in the peripheral blood of Pacific malaria patients 13 per cent. of the time and in Mediterranean patients about 10 per cent. of the time. In both groups, 75 to 80 per cent. of the time of parasitaemia was asymptomatic.

Norman H. Hise

SPITLER D. K. Malaria Relapse. Report of a Case Thirty-Six Years after Original Infection. *New England J of Med* 1948, June 10 v 238 No. 4 839.

The author describes the case of a Sicilian labourer of 69 years who had lived in the vicinity of Cleveland, Ohio for the previous 38 years. Previously he had been many years at sea and had called at ports as far as the South Pacific. He stated that he had had one attack of malaria in Sicily but could not recall his age at the time. He denied any recent hypodermic injections.

He was admitted to hospital complaining of fever "at 4-day intervals" and on that day and the next many *Plasmodium malariae* parasites were found in his blood. He was treated with quinine and made an uneventful recovery without further febrile illnesses. The author points out that in this case reinfection was highly improbable and that the case appears to have been a genuine relapse. The importance of keeping a diagnosis of malaria in mind in these cases is emphasized. Latency of this nature indicates the inadvisability of using as blood donors persons who have ever had malaria in the past.

It is suggested that the determining cause of the relapse in the present case may have been trauma, as the patient had fallen on the curb a few days before the onset of his chills, and struck the left side of the trunk, i.e. over the area of the spleen where he had a painful lump on admission.

H. J. O. D. Burke (Jury)

MARKER, J. RANG F. B. & HAINSTON, V. G. A Comparison of the Effectiveness of Quinacrine and Quinine against *Falciparum* Malaria. *Trans J T P Med.* 1948, May v 25 No. 3 401-4.

This work was carried out during the war in the 2/7 Australian General Hospital. Ninety nine patients with *P. falciparum* malaria were treated with quinacrine (mepacrine) and 104 with quinine. The course of treatment lasted 6 days in both groups. The daily doses were divided into 3 parts and were —

Quinacrine 1 2, 0.8, 0.4 0.4 0.4 0.4 grammes.

Quinine hydrochloride 40 40 40 30 30 30 grains.

Patients in both series responded rapidly to treatment. There was no appreciable difference between the two series as regards the rate of disappearance of fever or the rate of disappearance of parasites from the peripheral blood. There was no significant difference in gametocyte production in the two series.

Of the 99 patients treated with quinacrine 6 developed nervous symptoms 4 transient maniacal states and 2 epileptiform convulsions.

It was found that adequate plasma levels could be obtained when the total quinacrine administered was reduced from 3.6 to 3.6 gm.

Norman H. Hise

PARAMJOOTHY J. T. Notes on some Cases of Atebrin Psychosis. *Med. J. Malay.* 1947 Sept. v 2 No. 1 49-51

The author describes four cases of atebrin (mepacrine) psychosis in Malaya. The first was that of an Indian Mohammedan who suffered from malaria in 1944.

The author concludes as follows —

“ — A dosage of 300 mg given as a single dose was successful in resolving the clinical attack in 3 days in 81 to 87 per cent of cases in all types of infection both as regards fever and parasites ”

Parasitic relapses occurred after this treatment in all three infections

iii This trial was conducted at the Carmichael Medical College, Calcutta, on 20 patients suffering from clinical malaria with parasitaemia (10 *falciparum*, 6 *vivax*, and 4 mixed infections) These had had no antimalarial treatment for at least 6 weeks prior to treatment with paludrine The dosage employed in 6 cases (4 *falciparum*, and 2 *vivax*) was a single one of 100 mgm, and in the others 100 to 200 mgm daily for 2 to 5 days

The author gives the following summary —

“ — paludrine is a safe drug to use and will stop clinical attacks of malaria in doses which produce no untoward symptoms In the above series a minimum single dose of 100 mg, and a maximum of 700 mg, in five days were required to make the patient fever free and parasite free It had little effect on the sexual forms of the parasite — ”

iv This study was made at the Medical College Hospital, Calcutta, on 58 cases of malaria (20 *falciparum* and 38 *vivax*), with parasitaemia These were treated in 5 groups with doses of paludrine ranging from 600 mgm daily for 2 days followed by 300 mgm daily for 5-6 days [total 3,000 mgm] down to 200 mgm daily for 2 days only All were free of parasites by the 96th hour of treatment, but the pyrexia persisted in some cases beyond this, and was usually evident for a day or two after the blood had become negative

The author considers the drug “ an excellent and effective remedy ”, and thinks dosage must be continued after the peripheral blood is clear of parasites as the fever persists after this

v This work was done in the Sir J J Hospital, Bombay, on 50 cases of malaria with parasitaemia (26 *vivax*, 20 *falciparum*, 3 *malariae*, and 1 mixed) The dosage employed ranged from a single dose of 100 mgm to 600 mgm daily for 10 days [total 6,000 mgm] The variation in dosages had little influence on the immediate result, all attacks ending in a few days Subsequent dosage once weekly, it is suggested, “ could indefinitely prevent malarial infection from recurring ”

vi This study was undertaken in two isolated areas under the control of the Assam Railway and Trading Co, Ltd The experiment was to determine (1) a satisfactory suppressive dosage of paludrine in those not suffering from acute malaria and (2) the dosage necessary to control an acute attack of the disease In the first trial, a dose of 100 mgm of paludrine once a week was given as a prophylactic to 1,678 persons, 294 others untreated served as controls This dosage for various reasons was not found adequate, so 100 mgm of paludrine was then given twice weekly to 1,075 and 200 mgm once weekly to 800 persons, 246 remained untreated as controls Two hundred and thirty-five acute attacks of malaria (152 *falciparum*, 61 *vivax*, 15 *falciparum* + *vivax*, and 7 *malariae*) were treated with single doses of 100 mgm or of 300 mgm of paludrine, or with 200 mgm daily for two days

The author reaches the following conclusions —

1 As a suppressive, one tablet (100 mg) of paludrine once a week would probably be adequate, but when dealing with mass administration to a disinterested population a certain number are bound to miss the weekly dose for one reason or another One tablet (100 mg) twice a week reduces the chances of any one going a full fortnight without the tablet

2 The success of suppressive measures is directly proportional to the efficiency of the administrative controls

two days of treatment and did not reappear during the period of observation in the remaining 17 cases typical febrile attacks occurred at some time after the first five days of treatment. Asexual parasites disappeared from the peripheral blood after the first or second day of treatment. Gametocytes appeared in the blood of 51 of the 94 patients infected with *P. falciparum* after the 5th day of treatment.

*P. malar* parasites disappeared from the blood within 2 or 3 days of the beginning of treatment except in one case in which they persisted for 4 days.

In the *P. malariae* patient parasites persisted in the blood for 6 days.

Norma White

- i. SRIVASTAVA R. S. Final Report on the Field Trials of "Paludrine" in Selected Hyperendemic Malarious Areas of Naini Tal Tal in the United Provinces (11th September to 31st December 1946). *Indian J. Malariology* 1947 Sept. v 1 No. 3 361-3.
- ii. JAFAR, M. Preliminary Report on the Use of Paludrine in the Field. *Ibid* 365-8.
- iii. GHOSH B. N. Preliminary Report on the Result of Treatment of Malaria with Paludrine. *Ibid* 369-71.
- iv. DE M. N. & DATTA, P. N. Final Report on the Study of 53 Cases of Malaria treated with Paludrine. *Ibid* 373-81.
- v. PAREKH J. H. & BOGHANI B. P. Report on the Use of Paludrine Tablets. *Ibid* 383-7.
- vi. LOMAX, P. H. Paludrine Treatment Enquiry in Assam. *Ibid* 389-93.
- vii. AFRIIDI M. A. A Critical Review of Therapeutic Trials on Paludrine carried out in India during 1946. *Ibid* 347-60.

i. This trial was conducted in a village community. The dosage of paludrine employed was a single one of 300 mgm. administered by the medical officer personally. Alternate cases were treated with 300 mgm. of mepracrine daily for 3 days. During the period 11th September to 31st December 1946, 124 cases were treated: 8 with paludrine and 62 with mepracrine. Of the 8 paludrine-treated cases 37 were due to *P. falciparum* and 22 to *P. malar* while 17 showed no malaria parasites. Of the mepracrine treated cases 29 were *falciparum*, 20 *malar* and 1 *malariae*. 17 were blood negative.

From this observation the author concludes:—

"(I) Paludrine in the dosage in which it was administered (300 mg. single dose) controlled malarial attack quicker than mepracrine. The fever touched normal in 74 hours in 4 per cent of paludrine treated cases against 16 per cent of mepracrine-treated cases.

"(II) In an hyperendemic area like that of the Naini Tal Tal it is very difficult to evaluate the relapse preventing properties of paludrine because of the difficulty to ascertain whether a person had actually relapsed or had been reinfected. In the case which had a recurrence of fever in these areas were cases of relapse paludrine did not show any advantage over mepracrine in relapse-preventing percentage.

(III) No toxic effect were noticed.

ii. This trial was conducted in a hyperendemic malarial area in a rural setting 35 miles from Calcutta. A single dose of 300 mgm. of paludrine was given to adult patients a half or third of this to children under 1 year of age. All doses were given personally by the medical officer. Of the 49 patients treated only 16 had a parasitaemia (119 *falciparum*, 10 *malar*, 1 *malariae*). 17 *falciparum*, 13 *falciparum* *malariae* and 1 *malariae*).

The author concludes as follows —

“—— A dosage of 300 mg given as a single dose was successful in resolving the clinical attack in 3 days in 81 to 87 per cent of cases in all types of infection both as regards fever and parasites”

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“2 The success of suppressive measures is directly proportional to the efficiency of the administrative controls

"3. Three tablets (300 mg.) of paludrine will terminate a clinical attack and is as satisfactory from this point of view as two tablets (200 mg.) b.d. for two days."

vi. In the above series of papers are recorded the results of trials of paludrine in the field under varying conditions of life and of malarial endemicity in sundry parts of India and of Assam. These trials were conducted by independent workers at the request of the Malaria Institute of India, Delhi. In this paper Lt. Col. Afridi, Director of the Institute collates and analyses the data contained in them.

After a consideration of the characteristics of paludrine based on the reports of the original workers on the drug the author outlines the aim of the inquiry which briefly was to determine whether paludrine was effective against local strains of the malaria parasites (1) as a cure for clinical malaria, (2) as a radical cure of the infections, and (3) as a causal prophylactic or as a suppressive. The trials were conducted in rural dispensaries, in hospitals, in jails, and in tea estates and collieries details of these are analysed. On the whole acute *falciparum* infections responded more rapidly to treatment than did *vivax* there was some doubt about the response of *malariae* which the author believes on occasions to be delayed.

He concludes with the following summary —

1. Field trials on paludrine for the treatment of malaria were initiated in July 1946 in different parts of India under the direction of the Malaria Institute of India. The tests were carried out under varying conditions such as rural dispensaries, hospitals, jails tea estates and collieries. The result obtained up to December 1946 are analysed and reviewed critically.

"2. The value of different dosage regimes was assessed on 1991 microscopically diagnosed cases of malaria of which 1,200 were *falciparum* (malignant tertian) malaria, 481 were *vivax* (benign tertian) malaria, 66 were *malariae* (quartan) malaria while the remaining 59 cases showed mixed infections.

"3. Paludrine was found to be as effective against the strains of malaria parasites in India as those tested elsewhere.

"4. A single dose of 0.1 gm. and 0.3 gm. of paludrine effected a clinical cure within three days in 84.1 and 89 per cent. of cases. The drug was equally effective against the three species of malaria parasites although the response was more rapid in malignant tertian than in benign tertian or quartan. In trials where paludrine and mepracrine were tested side by side the curative action of paludrine in the above doses was equal to that of mepracrine in daily dose of 0.3 and 0.4 gm. for 3 and 4 days respectively.

"5. Neither the prolongation of treatment up to 10 days nor an increase in the dosage of paludrine to 0.6 gm. per day caused any appreciable improvement in the percentage of clinical cure. The re-admission rates caused by relapses and/or reinfections were relatively lower in cases treated with high dosages but none of the regimes tested appeared to effect a complete cure. A follow up treatment of 0.1 gm. once or twice weekly prevented the recurrence of disease in chronic relapsing cases.

"6. It is suggested that in the present state of our knowledge the most desirable course of treatment for malaria in India both in the dispensaries and the hospitals would be a single dose of 0.3 gm. of paludrine. In majority of cases relapses should be treated as and when they arise but for those who can be relied upon to take the drug regularly a follow-up treatment of 0.1 gm. once or twice a week should be prescribed for a minimum period of six months.

"7. Paludrine proved to be a safe drug, free from unpleasant effect and non-toxic even in high doses of 0.6 gm. per day. Patients placed on the drug experienced a feeling of well being within an hour or two of taking it. It was well tolerated by infants and pregnant women.



began on the 1st June 1946 and was continued to 25th November. Anophelines were very numerous after abundant winter and spring rainfall. The number of persons receiving suppressive drugs was 1,347, controls numbered 885. Of those given suppressive treatment, 331 received 0.3 gm. quinacrine (mepacrine) once a week, 312 were given 0.3 gm. nivaquine C (dihydrochloride) once a week, 166 were given 0.3 gm. nivaquine M (methylene bis-oxynaphthoate) twice a week, 129 received 0.3 gm. nivaquine M once a week, 31 received 0.1 gm. nivaquine M daily, 182 were given 0.3 gm. nivaquine C twice a week, 196 were given 0.1 gm. nivaquine C daily. All these doses were for adults only.

The results given by the two salts of nivaquine were comparable in every respect, but in view of the superiority of nivaquine C over nivaquine M in the treatment of malaria attacks the latter preparation might well be dispensed with. With a dose of 0.3 gm. once a week, the suppressive results obtained with nivaquine are in every respect as good as those obtained with the same dose of mepacrine. Nivaquine C, 0.1 gm. daily, gave remarkable results, the parasite index was reduced to zero whereas in an exactly comparable control area the parasite index rose from 4.65 to 10.98 per cent. Among the 84 persons in this control area there were 29 confirmed cases of malaria, there were none among the 196 taking a daily dose of nivaquine C. In no case was there any symptom of intolerance to nivaquine, in this respect the drug is certainly superior to mepacrine, nivaquine does not discolour the skin.

Norman White

McCULLOCH, R. N. & WATERHOUSE, D. F. *Laboratory and Field Tests of Mosquito Repellents*. Commonwealth of Australia Council for Sci. & Indust. Res. Bull. No 213. 28 pp. 1947. Melbourne.

The experiments were made during the recent war to find the best available mosquito repellent material for the fighting services exposed to malaria. Laboratory tests were conducted with the use of a tent containing large numbers of *Aedes notoscriptus* and *Aedes alboannulatus*. Other tests were made in cages with *Aedes aegypti* after a number of culicine species had been investigated for suitability. In the tent 1,000–2,000 adult mosquitoes were maintained, about 100 or so of which might attempt to bite at any time. The mosquito attack was severest at low levels, round the legs and ankles. Tent tests were presumed to be more like natural conditions but owing to the possible accumulation of vapour, only one or two materials could be tested in the tent per day. This involved the use of large numbers of insects. The cage tests employed much smaller numbers (100 or so), only an exposed arm surface was used. In both types of test, the time to first bite was considered very important but the intervals of subsequent bites were also considered in evaluating the repellents.

Field tests were done in New South Wales in coastal bush areas where *Aedes vigilax* was very common in places (biting untreated limbs at the rate of 25–50 per minute). Other tests were done in New Guinea where *Anopheles punctulatus farauti* and various culicines were the predominant biters.

The tests were made on more than 125 substances and some were tested at several dilutions. The most effective repellents giving nearly complete protection for 45 to 60 minutes under the most severe conditions, were Dimethyl phthalate, 612 (2-ethyl-1,3-hexane-diol), "Stayway" (diethylene glycol monobutyl ether acetate, etc.), oils of *Dacrydium franklinii* (Huon pine), *Melaleuca bracteata*, *Zieria smithii*, and *Backhousia myrtifolia*. Under similar conditions, Ceylon citronella oil gave protection for no more than twenty minutes.

CRAIG B. JR., WHORTON C. M., JONES R. Jr., PULLMAN T. V., ALVING A. S., EICHELBERGER, Lillian & ROGHMAN S. A Lichen-Planus-like Eruption occurring during the Course of Chloroquine Administration. / *Clinical Investigation*. 1943, May & 27 Vol. 3 Pt. 2, 36-9 4 figs. (10 refs.)

Of 130 healthy volunteers who were given chloroquine for one year in a dosage in excess of that required for antimalarial suppression two developed cutaneous eruptions simulating the rash occasionally caused by quinine. The patients had no serious systemic symptoms and the eruptions disappeared promptly when the drug was discontinued.

Three months after the end of chloroquine administration the drug was readministered to Case 1 at a dose of 0.3 gram a day for 17 days without reappearance of the eruption. Two months after the termination of the chronic toxicity study Case 2 resumed taking chloroquine in a dose of 0.3 gram twice a week. No cutaneous eruption developed in six months' drug administration.

SCHNEIDER, J., DIGBY M., VORON & SEAR M. Prophylaxie collective du paludisme par la premaline dans la région de Gabès (mai novembre 1944) [Mass Prophylaxis of Malaria with Premalins in the Gabès Area, May to November 1944.] *Bull. Soc. Path. Exot.* 1945 & 41 Nos. 3 & 4 194-8

Malaria had been particularly severe in the Gabès region of Tunisia in 1944 and 1945. The outbreak of *P. falciparum* malaria in the latter year was very serious, very few of the inhabitants either European or indigenous escaped malaria in 1945. The appearance of numerous new breeding places for *An. phlebotomus* and the extension of old breeding grounds were responsible for excessive mosquito prevalence. Pending the execution of large-scale anti-larval work it was decided to give suppressive treatment with premaline to the whole population numbering 3,500. Treatment was begun on the 1st May 1945. Of the confirmed cases on that date 67 in number were adequately treated. Erythrocytes received premaline 3 tablets for adults, once a week during the first month and thereafter every ten days till the end of November. (One tablet of premaline contains quinine 0.1 gm., rhodajume 0.003 gm. and procaine 0.003 gm. see DE ROUX *et al.* this Bulletin 1945 & 35 568). The results were satisfactory. The spleen index of children fell from 33.27 to 17.77 per cent and of adults from 10.77 to 6.5 per cent, during the period of drug administration. The fall in the parasite rate was from 14.21 to 0.61 per cent in children and from 8.87 to 1.25 per cent in adults. The total number of confirmed *verru* malaria during the whole season was but 77. 10 of these were in the hutana area where numerous normals who had arrived for the date harvest escaped prophylactic treatment.

There was not the least evidence of intolerance to the drug, among the 32,800 treated. Anopheles was at least as intense as it had been during the previous year when malaria was severely epidemic. *Norma* 11 figs.

SCHNEIDER, J., LURANI M. & BALTI M. Prophylaxie collective du paludisme par la nivaquine. Résultats de l'expérience de Ghardimaou (Tunisie) [Mass Prophylaxis of Malaria with Nivaquine. Results of Experience in Ghardimaou, Tunisia.] *Bull. Soc. Path. Exot.* 1945 & 41 Nos. 3 & 4 163-91

This paper gives the results of mass clinical prophylaxis of malaria with nivaquine, a synthetic product formerly named watoquine. This *Bulletin* 1945 & 45 148. The experiment was carried out in the region of Ghardimaou, Tunisia, where the population lives in small but stable scattered groups, farms or encampments, and is easy to keep under observation. Drug administration

TETZLAFF, F    **Operation of the United States Public Health Service Malaria Control Program** *Pub Health Rep* Wash 1948, Apr 30, v 63, No 18, 557-63, 2 figs

Before the war in some States of the U S A no malaria control organization existed, any activity in this direction forming part of the general sanitation programme. The wide extension of control measures during the war years by the Public Health Service of the Central Government to protect military personnel resulted in a more general recognition by the public of the value of these measures. Towards the end of the war, the application of DDT as a residual insecticide to control *A. quadrimaculatus* proved to be so effective that this method became the sole measure of control in many areas with the cessation of the older methods of drainage and use of larvicides.

After the war the situation of the war years was reversed in that it became necessary to protect the civilian population from malaria introduced by returning servicemen. Residual DDT spray operations have been extended to cover all affected areas in the United States. Coincident fly control has been a major factor in the general acceptance and success of the method. It is hoped that the expense entailed will be accepted eventually as a local charge on the rates, the end result should be a reduction in malaria incidence to the extent that malaria will no longer constitute a significant health problem in the United States. Lastly State and local Health Departments have become familiar with the programme necessary for the control of any insects having a public health significance.

R Ford Tredre

CORRADETTI, A    **Bases experimentales para la eliminacion de la malaria en la Costa del Peru** [Experimental Basis of Malaria Control on the Coast of Peru] Publicaciones de la Dirección General de Salud Publica Departamento de Malaria. 1947, Aug 7, 14 pp 2 graphs

The author describes the use of domestic spraying with DDT as a measure for the reduction of *Anopheles pseudopunctipennis* and malaria in the coastal plain of Peru.

It is known that in the coastal plain *A. punctipennis* is the principal vector it is only important when present in considerable numbers. The work was carried out in the valley of Mala, an area in which the Rockefeller Foundation has been studying malaria and applying other measures of control from 1942-46. The area was therefore a very suitable one for the experiment. DDT in kerosene was sprayed on walls of all houses in the valley at the rate of 2 gm per sq metre (apparently on a single occasion). The total human population of the area was 8,365. The Rockefeller Foundation had previously established that at the end of the transmission season the parasite rate was between 11 and 28.9 per cent. After the application of the DDT, the figure was always below 1 per cent at the same time of year. The greater part of the malaria was due to *P. vivax* but *P. falciparum* and *malariae* also occurred all three were very greatly reduced by the DDT.

The author states in somewhat general terms that the distribution of the DDT has been followed by a general reduction of mortality due to infectious diseases. He discusses the use of similar methods for the destruction of *Phlebotomus* and the control of verruga peruana.

P A Buxton

J NATIONAL MALARIA SOC 1948 June v 7 No 2 157-65 Cost Records in Malaria Control Report of the Committee on Sanitary Engineering [HENDERSON J M, Chairman]

The vegetable oils were rather unsatisfactory because they were inclined to be irritant to the skin. *Backhouse* and *Zeris* also have a pungent odour. "Stayway" is believed, on the basis of unpublished American work, to have a slight risk of toxicity danger to man. 612 has a distinct smell though in other respects is as good as dimethyl phthalate which was finally considered to be the best all round repellent.

Dimethyl phthalate is colourless, odourless and, apart from slight temporary smarting on application, is harmless to the skin. (Many thousands of men in the army have applied it for many months, often twice nightly without contracting dermatitis.) DMP was definitely better than most other phthalates (ethyl and butyl) tested, though a mixed methyl-ethyl phthalate was nearly as good. The treatment of clothing with dimethyl phthalate prevented mosquitoes biting through it for two or three days.

J. R. BULLING

BERGERIAN D. A. The Use of DDT Residual Spray in Malaria Control and its Effect on General Sanitation in Rural Districts. *J. Palestine Lab Med* 433 1948 Mar v 3 No. 3 49-61 1 map.

Two experiments were conducted in Lebanon in the Bekaa Plain between the Lebanon and the Anti-Lebanon mountain ranges. The object of the first was to observe the effect of residual DDT spray on the morbidity rates of various infectious fevers in two similar villages, two kilometres apart. All houses in one village were treated in the spring of 1945 and 75 per cent. of the houses in the second village were sprayed in the spring of 1946. The period of study was September and October 1946.

Tabulated results show that in the first village the number of cases of typhoid fever, fevers other than typhoid, diarrhoea, dysentery and conjunctivitis were 220 out of a population of 678 (34 per cent.) and in the second village 137 out of 687 (20 per cent.). The author's opinion is that there was no factor other than the DDT spraying to account for the lower morbidity rate in the more recently treated village (since the morbidity rates before spraying are not given there is no evidence to show that any alteration did in fact occur).

In the second experiment the object was to test the value of DDT residual spray in the control of malaria. Three highly malarious villages were selected. They are situated overlooking the plain and about a kilometre from the lake and a swampy area of Amuk. *Anopheles sachsi* is the chief anopheline but *A. superpictus* is also found. Preliminary observations were made on the abundance of breeding in the swamp and lake and on the spleen indices of the villagers. Then 5 per cent. DDT in kerosene was sprayed on the surface of the lake and in the houses. In treating the lake the vegetation was left and no attempt was made to reach the centre. Six sprayings were applied between May and November at intervals of 3 to 5 weeks. Each treatment was followed by a reduction in the numbers of larvae and in the numbers of adults in the houses. The numbers of other insects also diminished to remarkable extent but no ill effects on Gambusia or other fish were noted.

The author gives the costs of the experiment and describes methods and apparatus. He is satisfied that 5 per cent. DDT in kerosene is an effective larvicide even without the removal of aquatic vegetation and that residual spraying of dwellings resulted in the destruction of the insects associated with the dissemination of malaria, dengue, sandfly fever, conjunctivitis, summer diarrhoea of children, dysenteries and enteric and in highly malarious areas resulted in the reduction of the rates of parents of the inhabitants within a period of eight months.

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H. S. LARSEN

SIMPSON, M L. Reproduction of the "3T" Strain of *Plasmodium cathemerium* in White Pekin Ducks. *Am J Hyg* 1948, May, v 47, No 3, 315-31, 10 figs [19 refs]

This is the report of an elaborate and carefully controlled series of experiments on the cycle of *P. cathemerium* in the duck which deserved more interesting results than were actually obtained. The parasite was introduced by blood inoculation into (a) young ducks (two weeks old), (b) mature ducks and (c) canaries, and the ensuing infections were studied and compared. There was the same degree of synchronicity of segmentation in all three groups, viz. between 4 p.m. and 10 p.m. in a regular 24-hour cycle, unaffected by artificial conditions of lighting and darkness. In all birds, later in the disease, the synchronicity became less punctual. In canaries, segmentation was even more exactly timed and tended to occur 4 hours earlier in the day. The parasite density was greatest in young ducks and in the group exposed to artificially regulated light. The average number of merozoites per schizont was the same in all the ducks and throughout the 5 days of the patent period of the infection. In canaries, the number of merozoites varied during the course of the disease, probably because the patent period was lengthy and gave time for fluctuations to become manifest.

Late passage infections in ducks gave rise to fewer gametocytes than the earlier ones (a 6-fold decrease), indicating that long residence in the duck inhibited their production.

P C C Garnham

BOVET D, DECOURT, P, SCHNEIDER, J & MONTEZIN, G. Activité dans le paludisme aviaire de quelques dérivés synthétiques récemment introduits en thérapeutique: nivaquine, nivaquine B, paludrine et metachloridine. [Activity of Nivaquine, Nivaquine B, Paludrine and Metachloride in Avian Malaria.] *Bull Soc Path Exot* 1948 v 41 Nos 3/4 268-74 [16 refs]

## BLACKWATER FEVER

BLACK R H. The Resorption of Haemoglobin by the Renal Tubules in Haemoglobinuria. *Ann Trop Med & Parasit* 1948, Apr, v 42, No 1, 90-94, 12 figs on 2 pls [20 refs]

In man and some animals, conditions associated with haemoglobinuria often show eosinophilic granules in the epithelial cells of the convoluted tubules of the kidney. Such granules give the staining reactions characteristic of haemoglobin and are released into the lumen when the cells degenerate. The author suggests that haemoglobin in the glomerular filtrate is absorbed by the tubule cells and its nature modified in some way.

E T Renbourn

## TRYPANOSOMIASIS

GEIGY R. Beobachtungen an einer Zucht von *Glossina palpalis*. [A Note on a Culture of *Glossina palpalis*.] Reprinted from *Verhandlungen d. Schweiz. Naturforschenden Gesellschaft Zurich* 1946, pp 155-8.

The paper describes the maintenance of a culture of *Glossina palpalis* in Switzerland for a considerable period.

The author reviews what is known about the relation of *Glossina palpalis* to temperature. As it is established that at about 13°C the adult flies are quite torpid and capable of surviving unfed for 10-15 days, he decided to bring them

from the Congo to Switzerland in small gauze cages in an ice box. About 40 per cent. of the flies with which he started arrived alive, 22 males and 68 females reaching Basle. The original number has been increased to some extent by the importation of pupae but it seems that six generations were reared at the time of writing and that the number of flies was increasing. The insects were kept always at 26°C. and 83 per cent. relative humidity and were offered food daily on guineapage. Under these conditions one individual fly lived as long as 207 days and one female deposited sixteen larvae. The interval between the emergence from the pupa and the birth of the first larva is twenty-two days and after that births occur almost regularly at ten-day intervals. The duration of the pupal stage is thirty-five days in the female and about two days longer in the male. *P A B slow*

JACKSON, C. H. V. The Analysis of a Tsetse-Fly Population. III. In *E. genies* 1948 Apr v 14 Pt. 2, 91-103, 2 figs.

The author is concerned with the study and analysis of populations of *Glossina morsitans* at Hakoma, Tanganyika Territory. The main body of his material is derived from flies which were marked weekly for a long period and statistical deductions are here given from those results [see this *Bulletin* 1945 v 4, 186]. But the author has used a number of other ingenious methods of study and endeavours to check results obtained with one method against those of another. The present paper is stated to be the last of its series in it Jackson brings together some previous work, modifies certain of his methods and sets down his conclusions. For technical details the reader must refer to the original paper. Here it is only possible to make a brief and general abstract.

The bulk of the paper deals with the author's methods of calculating the actual population of twelve per square mile for which a new method is developed based on those individual flies which are marked and then recaptured more than once. He also recapitulates his work on the calculation of death rates and birth rates, subject on which he has developed a formula, assessing the errors of his estimates. His information on the disposal of individual flies is based not only on the familiar marking method but on unmarked flies introduced into a type of environment not unsuitable to *G. morsitans* though that species does not occur in it [see this *Bulletin* 1948 43-51]. The statistical work has revealed short term fluctuations in death rates and birth rates which cannot be associated with changes in climate and appears to depend on factors in the fly population. It seems that male *G. morsitans* are relatively inactive during the first ten weeks of life and that for that period their death rate may be lower than it is later. This inactivity, which has only recently been discovered, affects the shape of survival curves and the estimate of mean life expectancy, however still appears to be about four weeks for male flies. The fact that male flies are inactive early in life explains what has already been observed that if one estimates the age of a sample of wild flies by the wing, it overestimates the figure which is better than the estimation based on flies which are marked and recovered. The inactivity early in life has caused the author to make recalculation of his estimate of the whole male population; his previous estimates have to be increased by about 1.4 times. *P A B fast*

HILL, H. R. The Protein Content of Cerebrospinal Fluid in Trypanosomiasis. *Trans Roy Soc Trop Med & Hyg* 1948 Mar v 41 No 3 641-4 [16 refs.]

The most commonly used routine methods of protein estimation for cerebrospinal fluid depend on measurement either of precipitability as in the Oxford and Cantabrigia tests, or of specific gravity in some so-called turbidimetric test. The



is wide variability in the limits of normality given by different workers, even where the same methods are used. This is illustrated by the following figures, culled at random from various authorities —

Authors	Method	Normal C S F protein in mgm per 100 cc
MESTREZAT (1912)	Turbidimetric (Diaphanometric)	13-20
BUZZARD & GRENFIELD (1921)	, (Mestrezat)	-30
GREY (1930)	„ (Proteinometer)	-40
HARRISON (1939)	, (Mestrezat)	10-30
KING (1945)	, (Sulphosalicylic)	20-40
STITT <i>et al</i> (1945)	„ (Denis & Ayer)	15-40
PANTON & MARRACK (1945)	, (Sulphosalicylic)	20-35
HUTCHINSON & HUNTER (1934)	Precipitation (Aufrecht)	20-35
LEVINSON (1929)	, (Nissl s)	13-47
PURVES STEWART (1924)	, (Aufrecht)	20-30
SAUNDERS (1945)	, (Sicard & Cantaloube)	-22
French Trypanosomiasis Service	„ (Sicard & Cantaloube)	-22
Author	Turbidimetric (proteinometer)	20-30 (35)

Hill has performed an experiment in which three observers were asked to examine a number of cerebrospinal fluids both by the proteinometer and by the Sicard and Cantaloube methods. The former method consistently gave protein values  $1\frac{1}{2}$  to 2 times as great as the latter. Such a discrepancy would be very important where the proteinometer indicates 30 to 40 mgm per 100 cc, since according to SICARD and CANTALOUBE (*Bull et Mém Soc Méd Hôpit de Paris*, 1916, v 40, 481) this figure is grossly abnormal, and according to FAIRBAIRN [this *Bulletin*, 1934, v 31, 559] and SAUNDERS (personal communication) it has a bad prognosis in sleeping sickness, whereas according to GREY (*Arch Dis Childhood*, 1930, v 5, 187) and others, it is within normal limits, or perhaps, at the worst, at the upper limit of normal.

The author considers the Sicard and Cantaloube method to be the method of choice for routine work, since it gives a precipitate which lends itself to accurate measurement more readily than does opacity. Workers who refer to the protein content of cerebrospinal fluid should mention the method used.

[At the International Trypanosomiasis Conference at Brazzaville in February 1948, the recommendations of which are not yet published, it was concluded that the upper limits of the cell-count and total protein content of the cerebrospinal fluid within which a patient should be considered in the lymphatic-blood stage should be 3 cells per cmm and 0.025 gm protein per 100 cc, as estimated by the Sicard-Cantaloube method, that a more precise and, if possible, more rapid method for estimating total protein should be investigated, and that further investigation should be made into the exact composition of the cerebrospinal fluid in the normal African.]

E M Lourie

SALEUN, G & CHASSAIN, J. Premiers essais de traitement de la trypanosomase humaine, par la pentamidine en Afrique Équatoriale Française [First Trials of Pentamidine against Sleeping Sickness in French Equatorial Africa] *Bull Soc Path Exot* 1948, v 41, Nos 1/2, 89-104

This paper describes in detail the investigation of pentamidine for sleeping sickness, by a number of officers of the Institut Pasteur de Brazzaville and of

the recently established Service Général d'Hygiène M. biale et de Prophylaxie de l'A.E.F. See also TRINGUIER and ARABOULT this *Bulletin* 1948, v 45 313. The findings, at least in the main, confirmatory of work already published from other quarters. The first trials in A.E.F. were carried out at the Pasteur Institute in 1945 when 2 mgm./kgm. (whether dihydrochloride or di-bethionate is not stated) administered intravenously each day for 8-10 days was found to be too toxic. Dosage was then reduced to 1.25 mgm./kgm. for the first injection, 1.75 mgm. the next day, and 2 mgm. daily thereafter for the remainder of the course. Trials were then extended first to the "hypomeres" in various outlying districts, and finally to the itinerant treatment teams, where a disaster immediately occurred. The first three patients collapsed immediately after their first intravenous injection of 1 mgm./kgm. Two of these individuals recovered within 24 hours, but the third died after 7 minutes of coma and epileptiform convulsions. An error in the dosage actually administered cannot be excluded with certainty. Nevertheless it was decided to use only the intramuscular route of administration for ambulatory treatment in the future.

The toxic effects of treatment are described in great detail. As is well known the most common and most striking immediate effect is a considerable fall in blood-pressure occasionally associated with syncope. Transitory albuminuria occurred in only 3.7 per cent. of the cases treated. In only one instance was there the possibility that a significant degree of renal damage might have been due to the treatment. When the intramuscular route was used, toxic reactions were much less frequent and syncope never occurred, even when the dose was 3 mgm./kgm. It was found that pregnancy does not contraindicate the use of pentamidine (this is of interest in view of the statement not yet backed by much published evidence that propamidine tends to produce abortion see VAN HOOFF this *Bulletin* 1947, v 44 1048).

A treatment-course studied in many of the centres consisted of 8 daily injections, 8 days rest and then 8 daily injections again. When the first three intravenous doses were 1.0, 1.5 and 1.5 mgm./kgm. respectively it was sometimes 4 or 5 days before trypanosomes were no longer to be found, but where treatment was by 1.5 mgm./kgm. throughout it was nearly always the case that trypanosomes could no longer be seen on the day after the first injection. Where treatment began with the lower doses there was transient reappearance of trypanosomes between the 6th and the 11th injections in 4 of 84 cases. Where treatment was by 1.5 mgm./kgm. from the start this temporary reappearance of trypanosomes occurred in 1 of 61 cases. The authors therefore write that there is apparently a defined period when relapse tends to occur (a *periode de relapse*) during the actual course of treatment, which they say also characterizes the use of certain arsenicals.

In the first trials at the Pasteur Institute 16 of the 32 cases treated had advanced beyond the lymphatico-blood stage. All the other cases of this report to the number of 348 were in the lymphatico-blood stage. All were sterilized by the end of their treatment courses and were still well up to the limit of observation which in most cases, however, does not seem to have exceeded 6 months at the time of writing. There was a favourable response in all 125 cases which had previously proved to be refractory to other remedies such as suramin, tartar emetic and various arsenicals. E. M. LOURIE

Sick A. De quelques réactions au cours d'un traitement par la pentamidine.  
Some Reactions during a course of Pentamidine Treatment. *Bull. Soc. Path. Exot.* 1948, v 41 No. 3, 4 159-61

Mlle. W. R. aged 27 does not seem to have kindly let us attempt her very unusual case. She is apparently one of the two accidentally infected ladies about

whom SICÉ has already written, this *Bulletin*, 1948, v 45, 312] She was first treated by combined tartar emetic and atoxyl. This had to be stopped after a total of 250 mgm tartar emetic and 2.5 gm atoxyl, which caused pain along the veins chosen for injection, headache, and subjective visual disturbances. She then received suramin, first alone at a dosage of 1 gm, then in doses of 0.75 gm together with neo-stibosan. This gave rise to albuminuria, the appearance of leucocytes and blood casts in the urine, and hyperpyrexia. She was then given pentamidine isethionate in the gluteal regions, 150 mgm (i.e. 3 mgm per kgm body weight) daily. There was no particular reaction throughout the 8-day course of treatment, except for mild recrudescence of the renal disturbance. There was then a rest-period of 13 days, after which daily intramuscular injections were started again. At the 4th injection the patient developed a feeling of constriction in the throat, a bitter taste in the mouth, and a painful, tender, red swelling, about 5 cm in diameter and about 10 cm from the point of injection. It was freely movable under the skin. In the course of the next few days it assumed various colours and gradually subsided. Daily intramuscular treatment was, however, continued uninterruptedly in the scapular region without further complication, except for fleeting sensations of numbness down the limb on the side injected. The second treatment-course totalled 9 injections. [The tumour was non-fluctuant, but could it not have been a haematoma?] E M Lourie

TRINQUIER, E & PELLISSIER, A. Emploi du 3177 RP par voie buccale dans le traitement de la maladie du sommeil [Oral Treatment of Sleeping Sickness by 3177 RP] *Bull Soc Path Exot* 1948, v 41, Nos 3/4, 161-5

This report from the Brazzaville Pasteur Institute deals with the treatment of sleeping sickness by 2224 RP and 3177 RP, prepared by the Société Parisienne d'Expansion Chimique. [The compounds are identical, respectively, with melarsen (FRIEDHEIM, this *Bulletin*, 1941, v 38, 634) and melarsen oxide (WEINMAN and FRANZ, this *Bulletin*, 1946, v 43, 207, VAN HOOF, this *Bulletin*, 1947, v 44, 1048)]

Treatment was given orally. The first patient, who was in the nervous stage of infection, developed profuse diarrhoea after 2 doses of 30 mgm. The standard course of 3177 RP adopted for subsequent cases, therefore, consisted of 14 daily doses, comprising 1 of 10 mgm, followed by 4 of 20 mgm, and then 9 of 30 mgm per adult, irrespective of body weight. This was well tolerated in the lymphatico-blood stage (3 cases) and in the stage of meningeal reaction (5 cases) but not in the meningo-encephalitic stage (2 cases). As a result of the slight evidence obtained on a follow-up period of only 1 month the authors conclude that 3177 RP has a very rapid sterilizing action, that it can probably cure most cases in the lymphatico-blood stage, that it has no action in the stage of meningeal reaction, and that it is dangerous in the meningo-encephalitic stage.

In an addendum, benefit is claimed for 3 early cases treated by 2224 RP, also administered orally. E M Lourie

TRINQUIER, E & PELLISSIER, A. Emploi du 2224 RP par voie buccale dans le traitement de la maladie du sommeil [Oral Treatment of Sleeping Sickness by 2224 RP] *Bull Soc Path Exot* 1948, v 41, Nos 3/4, 260-68

Compound 2224 RP is identical with FRIEDHEIM's melarsen [see above].

Treatment was given orally in all cases. As a result of earlier findings by FRIEDHEIM and by MURAZ, which the authors describe, and after several unfavourable experiences with other dosages, the course finally adopted consisted of daily treatment for 2 weeks, beginning with 20 mgm/kgm the

first day rising by 10 mgm./kgm. daily, to 60 mgm./kgm. on the 5th day and maintained at this level for the remainder of the course but with a ceiling-dose of 3 gm. This was well supported in all the cases thus treated.

The gland-juice or blood was usually cleared of trypanosomes within 24 hours, but sometimes not until the fourth day. Symptoms rapidly abated in earlier cases, but sometimes became aggravated in the later stages of infection.

Cases treated consisted of 1 in the lymphatic-blood stage, 1 in the stage of meningeal reaction and 18 in the stage of meningo-encephalitis, 10 of which had proved resistant to earlier treatment with other compounds. The records given include results of cerebrospinal fluid examinations at the beginning at the end and 1 month after the end of treatment. The case in the lymphatic-blood stage responded well, and was still well 1 month after a single course of treatment but this was judged to be inadequate for the other types of case.

E. M. Lums

SALLES G. & CRASSAN J. Essai de chemo-prophylaxie de la trypanosomiose humaine en Afrique Equatoriale Française par la pentamidine. [Chemo-prophylaxis of Sleeping Sickness by Pentamidine in French Equatorial Africa.] *Bull. Soc. Path. Exot.* 1948, v 41 Nos. 3/4 165-8.

The authors report preliminary results of an experiment by CUOTURA and SOUVIAT in the Ouhanghi-Chari district of French Equatorial Africa.

On June 18th, 1948, the 409 inhabitants of 3 villages were examined 144 of these persons were already under observation after previous treatment for sleeping sickness, and 4 new cases were discovered. The remaining 261 persons were given a single intramuscular injection of pentamidine 4 mgm./kgm. for children (5-1 years, and 5 mgm./kgm. for those over 12 years of age.

The results of examinations at quarterly intervals, before and after this treatment were as follows —

Time of examination		New cases	Index of new cases
			Per cent
Before treatment	1st quarter 1948	28	5.7
	2nd	20	4.8
	3rd	4	1.09
	4th	10	3.2
	1st 1949	13	4.04
	2nd "	12	3.8
After treatment	3rd quarter 1948	2	0.9
	4th	0	0
	Jan Feb 1949	0	0

The authors therefore believe that single injection of pentamidine can protect for 4 to 8 months.

[The Index of New Cases is calculated as follows according to the International Trypanosomiasis Conference at Brazzaville February 1948 —

Total new cases 100

Total examined, less old cases considered not cured

E. M. Lums

- 1 LAUNOY, L & JEANPIERRE, C Essais sur l'action préventive du diamidino-diphénolypentane administré per os sur la trypanosomose expérimentale à *Trypanosoma equiperdum* du rat [Prophylactic Action of Oral Pentamidine against *T. equiperdum* Infection in the Rat] *Bull Soc Path Exot* 1948, v 41, Nos 1/2, 25-8
- ii — & — Suite à l'étude de l'action préventive du diamidino-diphénolypentane administré per os, sur la trypanosomose expérimentale à *Trypanosoma equiperdum* du rat [Further Studies of the Prophylactic Action of Oral Pentamidine in the Rat] *Ibid* v 41, Nos 3/4, 168-72

1 Thirty-six rats were given a single dose of pentamidine orally, over a dosage-range of 5 to 15 mgm per 100 gm body weight. There were 8 deaths from toxic action in the range 7.5-15 mgm, though most of the rats treated with 10 mgm withstood this amount. Each of the survivors received a single subcutaneous inoculation of 1 million *T. equiperdum* at intervals ranging from 5 to 20 days after treatment. The protective effects appeared in somewhat irregular manner. Complete protection for 7 days may, however, be expected after an oral dose of 5 mgm/100 gm. This is 10 times greater than the dose capable of protecting 50 per cent of rats for 14 days after subcutaneous administration [LAUNOY and LAGODSKY, *Bull Soc Path Exot*, 1940, v 33, 320, and this *Bulletin*, 1947, v 44, 702].

The therapeutic effect of oral treatment was also investigated. In heavy infections, doses up to 20 mgm/100 gm cleared the blood temporarily but did not cure. In earlier, light infections, there were 3 cures among 10 animals treated with 10 mgm/100 gm.

[There are two small errors in the authors' references to earlier work. WEINMAN and FRANZ (this *Bulletin*, 1946, v 43, 207) worked with melarsen oxide, not melarsen, and CLAESSENS (this *Bulletin*, 1947, v 44, 49) reported on propanidine, not pentamidine.]

ii The main burden of this contribution is to reduce the authors' previous estimate (see i above) of pentamidine's prophylactic powers. Further experiments, under the same conditions as above, showed that an oral dose of 10 mgm/kgm confers complete protection for only 4 or 5 days in only about 15 per cent of rats treated. E M Lourie

LAUNOY, L & CHABOUD, G, Mlle Des actions curative et preventive du diamidino diphénolypentane sur les infections à *Trypanosoma equinum* [Curative and Prophylactic Action of Pentamidine in *T. equinum* Infections] *C R Soc Biol* 1948 Apr, v 142, Nos 7/8, 432-3

Details are given of experiments in which pentamidine was shown to exercise curative and prophylactic effects against *T. equinum* in mice, rats and guinea-pigs. The trypanosome strain had been obtained from the Oswaldo Cruz Institute, Rio de Janeiro, in June 1947 but its previous history is not given. E M Lourie

VACHAN JONES, T G C A Short Survey of the Aims and Functions of the Game and Tsetse Control Department of Northern Rhodesia. Reprinted from *Rhodesia's Game and Tsetse* J 1948, 12 pp

The author gives a general readable account of problems of game pests and fisheries and of the method which is being developed by the Government of Northern Rhodesia for handling them. The author is Director of the Department of Game and Tsetse Control in that territory.

The subject is in itself very complex for in one place game may be an asset, in another a liability—so that there are conflicting interests between conservation and development of the territory or between the sportsman or the protectionist on one side and the pastoral or agricultural African on the other. Moreover different methods of studying the problems and dealing with them have been developed in different territories on the eastern side of Africa. It is certainly clear that it is wise to consider the whole of the wild life as a related group of problems and that these are important economically particularly in this large territory with a sparse population of people who are dependent to a great extent on food which they can themselves obtain or produce.

The Government of Northern Rhodesia started well by establishing the facts. They obtained the services of C. R. S. Pitman who produced a faunal survey published in 1934. In it he not only set down a mass of information about the animals and their distribution in the territory, but he also defined the main problems and suggested methods for their solution based on his own long experience in Uganda. Some of the immediate obvious problems are the control of elephant and of the ivory trade and development of what is required by the tourist and the sportsman—also the control of game in areas where it competes with cattle—the destruction of tsetse and the development of fisheries. The author in his position of Director of the Game and Tsetse Department of the territory has endeavoured to develop a unified view of these biological problems and a unified way of dealing with them. Here he has met with success partly it is believed because of his experience in administration in this country.

Two problems are of immediate concern to the readers of this *Bulletin*. The first is tsetse mainly *C. morsitans*. The policy of the Department has been to take the disease methods developed by neighbouring countries north and south and to make use of game exclusion or destruction and also of selective clearing in places where there were urgent tsetse problems. As two methods have been used it is not possible to state which is most effective but the general results are emphatically encouraging. The second problem is the risk of spread of rinderpest from Tanganyika and countries to the north into the Rhodesias. This was met partly by control of movement of cattle but also by destruction of game along a line which was approximately the southern frontier of the distribution of the disease.

The general tone of the paper is discreetly optimistic. One receives an impression that the author has thought very carefully about his group of problems, that some success has been won against the tsetse and that the prospect of adding wealth to the country directly or indirectly is considerable.

P. I. B. STON

TOMIE, Eleanor J. & REES, C. W. The Cultivation of *Trypanosoma cruzi* in Dialysate Medium. Research Notes. *J. Path. and Bact.* 1943, Apts. v 34 No. 162-3, 1 fig.

This note describes a medium prepared in loops of Cellophane tubing, by suspending them in the overlay of dialysate blood agar medium which is used for the routine cultivation of the organism. The stock medium consists of a blood agar made essentially as recommended by DE VRIES (this *Bulletin* 1941, 41, 348), that of this is overlaid with an equal quantity (10 cc.) of Lock's solution. For details of preparation and an illustration of the loop method the original paper should be consulted.

It is stated that *Trypanosoma cruzi* has been maintained in the dialysate medium for more than 3 years at temperature of 35°C. Bi-weekly serial transfers have been made from an inoculum of about one cc. of loop fluid containing active organisms. Growth has been good and the viability of the organisms has not decreased.

It is concluded that *T. cruzi* may thus be grown without proteins or other non-dialysable substances  
 H J O'D Burke-Gaffney

DÍAS E LARAJA F S & NOBREGA G Clínica y terapéutica de la enfermedad de Chagas [Clinical Characters and Treatment of Chagas's Disease] *Medicina Mexico* 1948, June 10 & 28 No 557 224-36

ROMANA C Profilaxis de la enfermedad de Chagas Ideas generales sobre el Tema [Observations on the Prophylaxis of Chagas's Disease] *Bol Oficina Sanitaria Panamericana* 1947 Nov-Dec & 26, Nos 11/12, 936-42  
 English summary

HAUSCHKA T S & GOODWIN, Margaret B *Trypanosoma cruzi* Endotoxin (KR) in the Treatment of Malignant Mouse Tumors *Science* 1948 June 4 600-602

### LEISHMANIASIS

SEN GUPTA, P C Observations on an Outbreak of Kala-Azar in Calcutta *Indian Med Gaz* 1947, Dec, v 82, No 12, 726-34, 5 graphs and 3 maps [10 refs]

In 1921 a kala azar out-patient clinic was opened at the Calcutta School of Tropical Medicine at this clinic data were collected which led to the observation by KNOWLES, NAPIER and DAS GUPTA in 1923 [this *Bulletin* 1923 v 20, 866] that kala azar was highly endemic in one quarter in Calcutta, whereas much of the town was comparatively free of infection. Intensive investigation in this quarter by these workers led to the first incrimination of the sandfly *Phlebotomus argentipes*, which subsequent investigation, culminating in the work of SWAMINATH, SHORTT and ANDERSON [*ibid*, 1943, v 40, 227] showed to be the vector.

This clinic has continued to operate, and in the years following the Bengal famine of 1943 an increase in the numbers and in the severity of the cases of kala azar was noted. Records of attendance of fresh cases show a rise to a high plateau in the years 1923, 1924 and 1925 (over 1,100 cases) with a gradual fall to 1930 (236 cases) and another increase in 1944 which culminated in a very sharp rise at the beginning of 1946. Distribution maps of indigenous cases in 1922-23 and 1942-43, respectively, show that little change occurred, but in 1946, although the old endemic area shows the greatest concentration of cases and the non-infected areas in the centre of the town are strikingly free still, there is a tendency for a centrifugal spread to the suburban areas that adjoin the endemic area. The increase in the severity of the disease is reflected in the frequency of complications, e.g., from 1935 to 1939 the incidence of cancrum oris was 1.7 per cent and from 1943 to 1946 7.1 per cent, and 5 cases of agranulocytosis occurred in 1946 and the first half of 1947, whereas this complication was not observed in Indian cases before 1942.

The factors which led to this increase were, the author considers, (i) the famine of 1943, at its worst from August to November, which caused widespread economic distress especially among the poorer sections of the population, (ii) the increased incidence of other diseases, cholera, smallpox, typhoid and malaria (iii) the population factor, i.e., the presence of susceptible material in the form of children born since the last epidemic wave and possibly (iv) an increase in the virulence of the parasite. "The indications are that, by the passage through this devitalized and highly susceptible population, the virulence

of the parasite was enhanced and the epidemic was maintained and progressed to the peak even when most of the other epidemiological factors had ceased to operate."

L. E. Napier

CHANG N. C. & HOU T. C. Cold Hemagglutinin in Chinese Kala Azar. *Proc Soc. Exper Biol. & Med.* 1948, May, v 68, No. 1 7<sup>th</sup>-4

Cold hemagglutinin in titers above 1:32 has been found in only 18.7% among 68 Chinese patients with kala azar. The highest titer obtained was 1:56. The titer bears no relationship to the severity, stage and treatment of the disease. Our results further suggest that there is no correlation between cold hemagglutinin titer and serum globulin content.

SEN GUPTA P. C., MALLIK K. N. B. & CHAKRAVARTY N. K. Observations on Pneumococcal Meningitis as a Complication of Kala-Azar. *Indian Med Gaz.* 1948 Jan. v 83 No. 1 8-11 2 figs, 1 pl.

The only reference to pneumococcal meningitis as a complication of kala azar that the authors were able to find was a statement by Rogers in his *Fetters the Tropics* (1919) that he found two instances in a series of 40 post mortem examinations in cases of kala azar.

The authors report four cases of kala azar in which a fatal pneumococcal meningitis occurred. The cases were encountered during the period of increased endemicity and increased severity of kala azar in Calcutta that followed the Bengal famine of 1943. All the patients were severely ill prior to the development of this fatal complication. In one case it was secondary to pneumonia, in one to cancerum oris, and in one to otitis media. In the fourth case no other focus was detected. All four patients were severely anaemic (haemoglobin 4.67 to 6.18 gm. per 100 cc.) and all but one had marked leucopenia (1,000 to 2,000) the exception was the patient with pneumonia (74,000). The cerebrospinal fluid was under only slight pressure. It was slightly hazy and not purulent, and there were only scanty pneumococci present.

The treatment given was penicillin intrathecally and intramuscularly. There was no response, and the fatal issue—within 74 to 93 hours of onset of symptoms—was not postponed. It was considered that the leucopenia explained the relatively low cell counts in the cerebrospinal fluid and the rapid course of the disease.

L. E. Napier

GHOSAL, S. M. & SINHA N. K. Trial of Pentamidine Isothionate in Kala-Azar Cases in the Patna Medical College Hospital (Preliminary Report). *Indian Med. Gaz.* 1948 Jan. v 83 No. 1 11-14

Treatment by pentamidine methosulphate was undertaken in 10 cases of kala azar in 10 of which the diagnosis had been made by the bone marrow aspirate in the sternal puncture smear. In the remainder the diagnosis was by the slide-culture test which was positive in every case.

The injections were given on alternate days intramuscularly. The first dose was 1 ml. the second 1.5 ml. and the third 1.5 ml. in a total dose of 4.5 ml. of 10 per cent solution. The weight of the patient was 100 lb. so that the maximum dose was 1 mgm. per lb. and

The results were judged on clinical basis. The temperature fell to normal after 5 to 6 days and within 6 days the leucocytes were well diminished. The patient felt hungry and the weight increased. In 10 patients the red cell count fell from 3,000,000 to 1,500,000 and in 10 cases rose to 3,000,000. The red cell count fell to 1,000,000 in 10 days although in some cases



improvement is recorded, no red cell count was over 4,100,000 and in 8 cases it is given as below 3,000,000 [There are no records of leucocyte counts]

The authors state that "No relapse was found in any of the cases so far observed" [They do not state if there was any form of follow-up of cases. In the paper there is no evidence that any case was followed for more than a few weeks after completion of treatment. However, this paper is called a preliminary report, so that further information may be given later]

There is no record of any ill-effects except bleeding from the needle track which was apparently troublesome in a few cases [In the title and the text isethionate is spelt "isothionate"] L E Napier

RANQUE, J, RANQUE, M, CABASSU, J & CABASSU, H *Le diagnostic precoce de la leishmaniose canine par la ponction ganglionnaire. Reflexions à propos de soixante examens positifs obtenus en dix mois dans la region marseillaise* [The Early Diagnosis of Canine Leishmaniasis by Gland Puncture. 60 Positive Results in Ten Months in the Marseilles Region] *Bull Acad Nat Méd* 1948, v 112, Nos 19/20, 339-40

Gland puncture in dogs can be carried out on a large scale, it is easy to perform, is acceptable to dog-owners, gives a satisfactory percentage of positive results and allows a very early diagnosis of canine leishmaniasis to be made before the clinical manifestations are clear.

In 94 dogs examined in the Marseilles area in 10 months, only 40 were clinically suspicious of leishmaniasis, and 6 were completely asymptomatic. Gland puncture revealed 60 positive, 29 negative and 5 doubtful results. In 46 formol reactions carried out in parallel, only 15 were frankly positive, 36 were negative and one was doubtful. In two dogs, leishmania were found in skin smears and in four others they were found at autopsy in the bone marrow, liver and spleen. The full results will be published later, but the authors make the following observations —

(1) Gland puncture gives the most significant results in the early stages of the disease, before the formal reaction or the clinical features are diagnostic.

(2) When the disease is established, the furfuraceous dermatitis and the positive formol reaction make the diagnosis simple but leishmania are far fewer in the glands and prolonged search may be required before they are found. If gland punctures are persistently negative, resort is had to smears from the skin, marrow, liver or spleen.

(3) In the final stages, the leishmania seem to be lysed in the glands, liver and spleen, but persist intact in the bone marrow in large numbers.

(4) In 20 cases, where a particularly early diagnosis was made by gland puncture, in the absence of any suspicious skin lesion, antimony treatment suddenly resulted in the appearance of the characteristic furfuraceous dermatitis and a spontaneous deterioration in the general condition. This new phenomenon is regarded as being analogous to the Herxheimer reaction in syphilis.

(5) Gland puncture has a prophylactic value, as it allows serial diagnoses to be made at the earliest stages when the disease is probably most contagious.

(6) Canine leishmaniasis is still as endemic around Marseilles as it was when PRINGAULT described it in 1914 [this *Bulletin*, 1914, v 4, 398].

H J O'D Burke-Gaffney

BOLLIGER, A & BACKHOUSE, T C *Transmission of Kala-Azar to the Australian Marsupials *Trichosurus vulpecula* and *Pseudocheirus lamgmosus** *Trans Roy Soc Trop Med & Hyg* 1948, May, v 41, No 6, 797-814, 14 figs on 4 pls [13 refs]

In an earlier paper ARMYTAGE & BOLLIGER [this *Bulletin*, 1945, v 42, 358] reported on their successful inoculation of *Leishmania donovani* to the pouch

young of the common Australian possum (*Trichosurus vulpecula*). In the present paper a full account of further experiments with twenty four possums and one ring-tailed possum (*Pseudocheirus lunatus*) is given. Twenty three of the twenty five animals including the ring tailed possum, became definitely infected. The animals were of all ages. Pouched young remained longer in the pouch up to 6 months instead of the usual 3 or 4 months, and showed stunted growth and fine grey woolly fur. The time of survival varied from 81 to 704 days. Some of the larger animals which survived infection for over a year showed no immediate effects of the infection for several months apart from a transient conjunctivitis and other eye changes. Loss of weight or failure of the growing animal to increase normally was one of the earlier signs of infection. The fur changed to a fine woolly structure. Occasionally necrotic skin lesions appeared temporarily near the root of the tail.

In the majority of possums serious eye changes occurred. Apart from the conjunctivitis, which cleared up after a few weeks or months the cornea became hazy and iris developed. The haziness was due to small whitish dots adhering to the posterior aspect of the cornea. Increasing keratitis giving the cornea a bluish-white opaque appearance might seriously or completely impair the sight. The iris showed a tendency to adhere to the lens. In some cases corneal abrasions, scars and haemorrhage into the iris were noted.

Advanced kala azar produces marked degeneration of the testes. This is manifest by diminution in size and alteration in spermatogenesis. The testes may be only a half or a third of their normal size while abnormal spermatozoa are produced or complete cessation of spermatogenesis may occur. In the majority of females, the pouch and mammary glands are found to atrophy. The pituitary and suprarenals were generally smaller than normal and frequently contained parasites so that the genital atrophy and stunted growth may have been caused by interference with the gonadotropins and growth hormones. In the brain and spinal cord the lesions take the form of a dense invasion of the pia-arachnoid with lymphoid cells, and perivascular infiltration in the cerebral cortex and grey matter of the cord. There is marked proliferation of astrocytic cells around the cortical capillaries and many of them include parasites. In most animals the spleen is enlarged but in three it was reduced in size. Generally the size of the liver fell within normal limits, though excessively large livers occurred as well as small ones. The kidneys appeared normal but in half the animals parasitized cells occurred. In one animal parasites occurred in cells of the renal tubules. Parasites were present in all the organs after the single injection intraperitoneally or intracardially. Blood from another infected animal of culture or of bone marrow from a human case.

It is evident that the Australian marsupial the possum, is highly susceptible to kala azar and will be a suitable animal for investigation of the disease in that country. The details of the history and histological findings in three of the cases are given while the appearance of the abdominal organs in two cases as shown in photographs and histological findings are illustrated by twelve micrographs.

C. M. S. YOUNG

HERING M. & FAIRCHILD G. H. The Control of Phlebotomus in Peru with DDT. Amer J Trop Med 1948 Mar v 28, No. 3, 257-301 map & 4 figs on - 54.

The authors, both of whom are authorities on the entomological side of the subject give an account of the control of *Phlebotomus* in Peru with DDT together with number of valuable notes on the biology of these insects.

Preliminary work in the Mediterranean had shown that spraying houses with DDT in kerosene results in a very great reduction in nuisance from similar and

in the number of specimens of *Phlebotomus* which can be caught, though there was no reduction in untreated buildings in the neighbourhood

The work here described was carried out in 1945 in Peru, a country in which *Phlebotomus* is of great importance as a vector of human disease. The authors worked in the Rimac Valley at a little over 6,000 ft in places where *Phlebotomus verrucarum* predominated. They estimated the number of these insects by catching them in houses, stables, poultry houses, caves and cavities in stone walls, driving them out with tobacco smoke and observing them with an electric torch. They also estimated their abundance by the number of the characteristic bites on human beings, and by reports about annoyance from these insects. They also appear to have placed considerable reliance on what they describe as the "Burro rate" - we are inclined to suppose that this must refer to the number of sandflies biting a donkey (*Equus asinus*).

The authors' standard application was a 5 per cent solution of DDT in kerosene sprayed at the rate of one gallon per thousand square feet on walls of houses, cavities in dry stone walls and so forth. The results are fully presented and discussed and are accompanied by photographs showing the type of building and of country, and plans showing which houses or walls were or were not sprayed in certain villages. It was found repeatedly that if a room or stable was adequately sprayed it was rare to find any sandflies or obtain any report of biting for several months - this, as the authors remark, would cover the whole sandfly season in many parts of the world. Even spraying the outside of a mud house is fairly effective and spraying the spaces in a dry stone wall is also effective. It seems then that with DDT applied in this way, one may not only suppose that a large number of sandflies are killed but one has a sort of barrier between the insect and the human inhabitants. The authors also point out that as the life cycle of *Phlebotomus* is long a sandfly population would only build itself up again very slowly after being greatly reduced by DDT [a point which one would like to see considered in relation to some population statistics]. As in other parts of the world, it was clear that the sandflies were flying a very short distance for they were discovered in numbers between 75 and 200 yards from the sprayed structures, provided suitable shelter was available. A point of interest in the present paper is that unlike much work on insecticides it pays very full attention to the biology of the insect.

The authors have also considered their results in relation to the spread of diseases transmitted by *Phlebotomus*. They controlled the insect in two large construction camps, and this was followed by an almost complete cessation of new cases of cutaneous leishmaniasis and bartonellosis.

P A Buxton

## FEVERS OF THE TYPHUS GROUP

GROENENDIJK H J Die *Rickettsia prowazeki* im bebrüteten Hühnerei [*Rickettsia prowazeki* in Egg Culture] *Ztschr f Hyg u Infektionskr* 1944 Nov 12 v 126 Nos 1/2 170-78

GIROUD P & CIACCIO G Valeur de divers extraits pulmonaires de lapin infecté de *Rickettsia prowazeki*, jugée par l'agglutination des rickettsies [The Estimation by *Rickettsia*-Agglutination Tests of the Potency of Various Extracts of the Lungs of Rabbits inoculated with *Rickettsia prowazeki*] *Bull Soc Path Exot* 1948, v 41, Nos 3/4, 117-20 [10 refs]

Soluble antigens were obtained from the lungs of rabbits infected with *Rickettsia prowazeki*, by extraction with ethyl alcohol, methyl alcohol, dilute glycerin, saline solutions, and distilled water

The potency of the extracts was tested by inoculating rabbits with them and afterwards estimating the titre of complement fixation tests carried out on the animals' serum.

The alcoholic extracts caused more rapid responses than the others, and when dehydrated *in vacuo* at  $-40^{\circ}\text{C}$ . retained their full antigenic power for at least 30 days.

John H. D. McGraw

BILLING R. & OTLENICHS Lilly. Untersuchungen über die Fleckfieberinfektion beim Kaninchen. [Investigation of Typhus-Fever Infection in Rabbits.] *Ztschr f Hyg u Infektionskr* 1947 Jan. 6 v. 177 Nos. 1/2, 13-28.

This is a study of the reaction described by GIROUD (this Bulletin 1938 35-790) as resulting from the intracutaneous injection of typhus rickettsiae into rabbits.

After a series of careful experiments the authors concluded that the intensity of the reaction in strictly controlled conditions could serve as a measure of the antigenic potency of suspensions containing living rickettsiae and therefore also of the suitability of the suspensions for the preparation of vaccines. Yolk sac material was regarded as suitable when it caused a definite reaction in dilutions of 1:10,000 to 1:100,000. With fresh suspension the index (potency based on the reaction) was parallel with the richness of the suspensions in rickettsiae.

With killed suspensions very rich in rickettsiae an early mild reaction occurred owing to the presence of endotoxins; a similar reaction might also occur with living rickettsiae but in this case it was followed by the more severe reaction resulting from the multiplication of the rickettsiae in the skin.

John H. D. McGraw

BILLING R. & OTLENICHS Lilly. Untersuchungen über aktive und passive Fleckfieberimmunität bei Kaninchen. [Investigation of Active and Passive Immunity against Typhus Fever in Rabbits.] *Ztschr f Hyg u. Infektionskr* 1947 Jan. 6 v. 177 Nos. 1/2, 29-40.

Continuing their study of the Girooud reaction the authors found that a pronounced degree of active immunity against further intracutaneous inoculation with homologous rickettsiae was produced within seven days in rabbits which had been inoculated intracutaneously with large doses of yolk sac suspensions containing living rickettsiae.

An appreciable degree of immunity was also caused by injections of killed suspensions, but then the immunity was not pronounced and the occurrence of allergic reactions due to the yolk sac material was more marked. It follows that the reaction was not considered suitable for use in the practical testing of vaccines. Allergic reactions could however be prevented by using rickettsial suspensions of different origin for the second inoculation—for example lung suspensions obtained from rabbits after several lung passages of infection. By this procedure all trace of the original yolk sac material was removed.

The potency of rickettsial vaccines could be measured by finding the quantity of immune serum needed to prevent the occurrence of the Girooud reaction and then comparing this with the quantity of the same serum needed to prevent the reaction when a vaccine of known potency was employed in the same way.

John H. D. McGraw

SFORZA, M Sul contenuto in agglutinine normali Antiproteus OX19 e OX2 in individui residenti in Eritrea [Agglutinins against *Proteus* OX19 and OX2 normally occurring among Residents in Eritrea] *Boll Soc Ital di Med e Igiene Trop* (Sez Eritrea) 1947, v 7, Nos 5/6, 464-74 [11 refs] English summary (7 lines)

Weil-Felix tests were carried out on groups of healthy persons in Eritrea before and after the epidemic of 1946 Before the epidemic season the percentage of reactions against *Proteus* OX19 at titres of 1-160 and 1-320 were — Among Italians 1 17, hill-country natives 8 2, and lowland natives 6 7 After the epidemic the corresponding figures were 13 2, 21 7 and 18 9

Comparative tests with *Proteus* OX2 were carried out only during the post-epidemic season, titres higher than those observed with OX19 occurred in 17 per cent of the Italians, in 8 per cent of the hill-country natives and in 18 per cent of the lowland natives, so the reactions were mostly of the OX19 type

John W D Megaw

MORGAN, H R, NEVA, F A, FAHEY, R J & FINLAND, M Brill's Disease Report of Two serologically proved Cases of Typhus Fever in Irish-Born Residents of Boston *New England J of Med* 1948, June 17, v 238, No 25, 871-3, 2 figs

Two cases of typhus fever, serologically confirmed as being of the epidemic or louse-borne type, occurred in Boston in September 1946 and October 1947 The clinical features conformed to the pattern observed in Brill's disease

Both of the patients had lived in County Galway, Ireland, till they emigrated to Boston, one in 1910 at the age of 20, the other in 1913, at the age of 17 In 1903 a serious epidemic of typhus fever occurred in County Galway when the patients were 13 and 7 years of age

Complement-fixation and rickettsia-agglutination tests were carried out by Herald R Cox and J E Smadel, both of whom regarded the results as diagnostic of epidemic typhus In both cases the complement-fixation titres against epidemic antigen were two to eight times higher than those against murine antigen in the repeated tests that were carried out The epidemic titre rose to 1-2,560 in each case The results with the agglutination tests were less convincing, but when a difference in titre occurred the epidemic titre was always higher than the murine

It appeared most likely that both of the patients had suffered from Brill's disease, the form of louse-borne typhus that occurs as a recrudescence of a latent infection persisting indefinitely after an attack of louse-borne typhus

John W D Megaw

SCHMIEDER, F Das Encephalogramm nach Fleckfieber [The Encephalogram after Typhus Fever] *Klin Woch* 1948, Jan 1, v 26, Nos 1/2, 14-19, 12 figs.

The author describes the findings obtained by encephalography in 44 cases of after-effects of attacks of typhus fever which had occurred one to three years previously The paper is illustrated by 12 excellent photographs.

The patients were not selected because of the special severity of their signs and symptoms their disabilities ranged from hemiplegia with pronounced psychosis to trivial neurological manifestations.

In two-thirds of the cases, some abnormality was detected this usually consisted in enlargement or deformity of the third ventricle There was no definite correlation between the X-ray findings and the clinical features, but the author claims that the occurrence of an abnormality in the encephalogram

of a given patient increased the probability that his psychic or neurological defects had resulted from a previous attack of typhus fever. The procedure was therefore considered to be of diagnostic value.

In three cases it was found impossible to introduce air into the third ventricles, even after repeated attempts.

The author is doubtless justified in claiming that this is the first occasion on which cephalography has been employed in a systematic manner in the investigation of the persistent after-effects of typhus fever.

J. H. D. McNE

D'IGNAZIO, C. Il problema del dermatofilo e della lotta contro il dermatofilo in Etiopia (1938-1946) [The Problem of Typhus Fever and its Control in Ethiopia (1938-1946)]. *Boll. Soc. Ital. di Med. e Ig. Trop. (Ser. Eritrea)*, 1947, 7, No. 58, 423-9.

In this paper it is stated that the case-fatality rate of typhus fever (house-borne) among Europeans in Ethiopia fell from 25-30 per cent. in 1937-1938 to 0.5 per cent. for the five years 1941-1946.

The causes of this astonishing fall are discussed, but even making the fullest allowance for early diagnosis, better methods of treatment and a progressive decline in the virulence of the infection, the author feels compelled to fall back on the theory that the control measures, such as improvements in hygienic conditions, house control, and the use of vaccines, have not only increased the resisting powers of the individual but also have produced a durable attenuation of the virulence of the rickettsiae through interference with the chain of transmission and adverse biological effects on the lice.

J. H. D. McNE

DAVIS, D. E. Observations on Rats and Typhus Fever in San Antonio, Tex. *Pub. Health Rep. Wash.*, 1948, June 11, v. 63, No. 4, 783-91, figs.

The author presents information on the composition of populations of rats (*R. rattus* and *R. norvegicus*) at San Antonio, Texas, and on the presence of typhus antibodies in them.

San Antonio lies about 30° N. that is to say outside the tropics. The climate is classed as humid sub-tropical. The average rainfall is 28.9 inches and rain generally falls in every month of the year. The mean temperatures over a series of years range from 63°F. in January to 84°F. in July and August.

The paper contains information on such matters as the length of head and body of the two species classified by sex and age, the criteria for age being based on the reproductive condition, also on the sex ratio of trapped and poisoned rats. It seems that reproduction occurs throughout the year with a maximum in the period May to June.

The presence of typhus antibodies was determined by complement fixation. In adult *R. rattus* 34 per cent. were positive and in adult *R. norvegicus* 51.4 per cent. Rats from grain mills are more frequently positive than those from houses or stores and the difference is highly significant in statistical sense.

J. H. D. McNE

SAVOUR, S. R., VARIA, V. S., SUMAN, D. W. Typhus in Bombay. Part I. Clinical Features. *Ann. Varia & Soma. Ind. Med.* 1948, Jan. 1, 23, No. 1, 1-4, 11-15. Part II. Epidemiology. *Ann. Varia & Soma. Ind. Med.* 5, 3.

During the years 1944 and 1945 more than 200 cases have been diagnosed as epidemic louse-borne typhus on the strength of Widal test reactions, presumably of the 1/4 and 0.1/10 type at titres 1/1 and 0 or over.

It was possible to study 70 of these cases at hospitals in Bombay City. The average duration of the fever was 12 days, a rash was seen in 24 per cent of the cases, and the fatality rate was 2.8 per cent.

The incidence was greater in the first half of the year than in the second, there was a sudden drop in the number of cases in July and a further decline in August, flooding out of the rats by the monsoon rains was regarded as the probable cause of the low incidence during these months.

Five strains of rickettsiae were recovered from patients and another strain was recovered from one out of six rats captured in a house in which a case had occurred, a description of these strains will be given in a later paper.

No body lice were found on any of the hospital patients. The clinical and epidemiological features of the disease as described are consistent with the diagnosis of flea-borne typhus.

In an Appendix, a description is given of a new modification of the rapid slide test. The alcohol-killed suspensions of *Proteus OX19*, as supplied by the chief laboratories in India for the Weil-Felix test, are concentrated by keeping the bottles or ampoules in the ice-chest for five days and then removing the upper, relatively clear, two-thirds of the liquid with a pipette. To the remaining suspension a "small crystal" of sodium citrate and a drop of Loeffler's blue are added.

One drop of the suspension and a drop of the patient's blood are mixed on a slide which is gently rocked and a watch is kept for the occurrence of agglutination. The method was tested on 250 samples of blood whose Weil-Felix titres were known and it was found that clumping within ten seconds corresponded with titres of 1-500 or over, clumping within half a minute corresponded with a titre of 1-250, and within a minute with a titre of 1-125. When clumping was delayed beyond a minute, the result was of doubtful significance.

John W D Megaw

Fox, J P The Long Persistence of *Rickettsia orientalis* in the Blood and Tissues of Infected Animals *J Immunology* 1948, June, v 59, No 2, 109-14 [15 refs]

*Rickettsia orientalis* was recovered by mouse inoculation from the tissues of Swiss mice up to 610 days after experimental infection. Most of the mice had recovered from heavy doses of infection because of being treated with toluidine blue or methylene blue. The kidneys were the most infective organs, next came the brain and liver, the blood was less virulent because of the presence of antibodies. The urine was tested for infectivity on two occasions, with negative results.

Cotton rats were found to harbour infection in the blood and tissues up to the 102nd day after infection, the blood ceased to be infective by the 154th day, and the brain by the 269th, when the kidneys were still infective.

The author states that "the significance of these observations to the problem of the rodent reservoir in tsutsugamushi disease is obvious".

John W D Megaw

NOURY, M Sensibilité du mérion (*Meriones shawi* Lataste) au virus du typhus tropical [Susceptibility of the Rodent, *Meriones shawi*, to the Rickettsiae of Tropical [Mite-borne] Typhus] *Bull Soc Path Exot* 1948, v 41, Nos 3/4, 115-17

A Moroccan rodent, *Meriones shawi*, was found to be at least as susceptible to intraperitoneal inoculation with *Rickettsia orientalis* as the closely related gerbille (*Gerbillus gerbillus*, *G pyramidum*) which has been regarded as the animal of choice for experiments with the organism.

John W D Megaw

SOMAN D W & DAS MENON V K. Scrub Typhus (Mite Typhus) in Bombay with a Report on the Isolation of Canine Rickettsia. *Indian Med. Gaz.* 1948 Jan v 83 No. 1 17 20 4 figs on 1 pl.

Weil-Felix reactions of the Proteus OVA type were observed in sera from 16 among a large number of pyrexial patients in Bombay City during the year 1948. Rickettsiae were recovered by mouse inoculation from 8 of the 12 patients investigated. The organisms were similar to *Rickettsia cynopteri* in their morphology in the reactions produced in mice and in the effects of intra-ocular inoculation of rabbits. There was also evidence of cross-immunity against a Ceylon strain of *R. orientalis*.

In 7 of the 12 patients an eschar was observed and in 6 there was a rash. Fourteen of the 16 cases occurred in the months September October and November.

Special attention is called to the occurrence of scrub typhus in even a metropolitan city like Bombay. (SOMAN *et al.* this Bulletin 1948, v 45 81) has pointed out that contact with mite-infested vegetation is liable to occur in Bombay. John H. D. McGarr

SPORZA M. Dermotite in Eritrea. (Identificazione del virus storico murino e da zecche) Typhus Fever in Eritrea. Identification of Epidemic, Murine, and Tick-borne Strains of Rickettsia. *Ital Soc. Ital. di M. d. e Ig. T. p. (L. Eritrea)* 1947 v 7 No. 4 6 43-52.

Details are given of the isolation and investigation of two strains of rickettsiae of epidemic typhus and of one strain of the murine type but most of the paper is devoted to a description of a number of strains of tick typhus infection.

Three tick typhus strains were isolated from patients, three from ticks collected from dogs belonging to patients, and one from the brain of a dog which harboured infected ticks. The ticks concerned were *H. parva* and *R. p. eurasianus*. Two ticks of the latter species obtained from an infected dog were allowed to feed on a guinea pig, which in due course yielded strain of rickettsiae.

Three strains of tick typhus rickettsiae were thoroughly studied by passage through guinea pigs and inoculation into the eye of rabbits, with the result that cross immunity against the other two strains but none demonstrated against epidemic or murine strains.

An outbreak of tick typhus is described in which ten persons living in a tick-infested area at an altitude of 858 m. were attacked, four of the patients had inoculation eschars. The Weil-Felix reactions were irregular in most cases Proteus OVA gave higher titration than P. OX but in one case there was an OX reaction of 1/320 and certain reaction with OVA and in one case the OVA reaction was 1/160 as compared with reactions at 1/40 with the other two organisms.

The author concludes that the tick typhus of Eritrea is more closely related to boutonneuse fever but it cannot be told that the causative organisms are identifiable with *Rickettsia cynopteri*. John H. D. McGarr

SPORZA M & SOLINAS N. La reazione di Weil-Felix sul siero di sangue dei cani di Asmara. Weil-Felix Reactions in the Dogs of Asmara. *Riv. Soc. Ital. di M. d. e Ig. T. p. (L. Eritrea)* 1947 v 7 No. 5 6 47-52. (In Italian summary 18 lines)

Among 159 dogs captured at random in Asmara the following Weil-Felix titres were observed:—



	1-640	1-320	1-160	1-80	1-40	Negative
Against <i>Proteus</i> OX19	1	6	13	50	47	42
„ <i>Proteus</i> OX2	0	6	9	58	32	54

In the absence of reliable evidence the authors arbitrarily adopt a titre of 1-320 or over as evidence of the existence of rickettsial infection, this is the same standard as has been adopted for human beings

John W D Megaw

STREETEN, G E W, COHEN, R S, GUTTERIDGE, N M, WILMER, N B, BROWN, H E, SMITH, D J W & DERRICK, E H Tick Typhus in South Queensland Report of Three Cases *Med J Australia* 1948, Mar 20, v 1, No 12, 372-3

In two of the three cases described in this paper, there was a history of bite by a tick ten days or less before the onset of the fever. From the description given by the patients the tick was probably *Ixodes holocyclus*. In the third case there was no evidence of a bite but the patient had recently been walking in a "scrub area". In every case there was an eschar and lymphadenitis. The clinical features were consistent with the descriptions by ANDREW *et al* of tick typhus in North Queensland [this *Bulletin*, 1947, v 44, 202].

In one of the cases with a history of tick bite the Weil-Felix titres were *Proteus* OX19, 1-640, P OX2, 1-320, and P OXK negative. In the other case with tick bite the OX2 reaction was not tested the OX19 titre was 1-160 and the OXK reaction was negative. In the case without history of tick bite the OX19 titre was 1-320, the OX2 and OXK titre was 1-40.

The authors think it likely that in the past a number of cases of tick typhus have been regarded as murine typhus because of a positive reaction against *Proteus* OX19

John W D Megaw

PAYZIN, S & GOLEM S B Türkiye de Q humması (Rapor I) [The Presence of Q Fever in Turkey] *Türk İhtiyat ve Tecrübe Bilyoloji Dergisi* Ankara 1948 v 8, No 1, 94-113, 8 figs on 4 pls [12 refs] English summary p 116

The authors inoculated 24 guinea-pigs intraperitoneally with blood from 16 patients who had clinical atypical pneumonia. 7 of the animals developed pyrexia and were killed and examined post-mortem, their spleens were enlarged and *Rickettsia burneti* was recovered from them.

Complement fixation tests with Q fever antigen obtained from the Rocky Mountain Laboratory, were performed on 100 specimens of serum from patients having atypical pneumonia. 24 of these were positive at titres of 1/10 to 1/320.

Positive results were also obtained, however, in 13 of 115 sera sent for the Wassermann reaction (including 4 which also gave a positive W.R.), but the titre only exceeded 1/40 in one case.

Sixty specimens of serum from domestic animals were examined by the complement fixation test and 13 were positive.

The authors are pursuing the question of a possible relation between Q fever and contagious pleuro-pneumonia in goats

H J O'D Burke-Gaffney

LENGRAND J Nouvelle observation de Q fever faite dans les environs d Alger [Another Case of Q Fever Observed in the Vicinity of Algiers] *Bull Acad Nat Med* 1948 v 132 Nos 13/14 251-3 1 chart

DE RICK, ENRIQUE & RODRIGUEZ, A. Fiebre "Q." Reporte de un caso (with brief histological study of a case of Q fever) Arch. Hospital San Juan 1947 July-Dec v 2, Nos. 3 & 4 37-44, 10 figs. 33 refs.

ROSOFF, L., WEST, H. E. & BOWEN, A. G. Q Fever: Case treated with Streptomycin. J. Intern. Med. 1948, June v 28 No. 6 1187-92, 3 figs. 14 refs.

Q fever has recently been identified in the Arleta area of Los Angeles County. A case of Q fever is reported here with clinical and roentgenographic findings consistent with this diagnosis and confirmed by positive complement fixation tests. Treatment with streptomycin was instituted and proved satisfactory although further clinical investigation is necessary to establish its efficacy in this disease.

BLANC, G., BRUNEAU, J., POITROT, R. & DELAGE, B. Quèquies données sur la Q fever (maladie de Derrick Burnet) expérimentale. (Some Findings in Experimental Q Fever) Bull. Acad. Nat. M. d. 1948 v 132, Nos. 13 & 14 243-50, 4 figs.

The authors describe the results of a considerable number of experiments, carried out primarily as a therapeutic measure in which patients (presumably suffering from mental disease) were inoculated with the rickettsiae of Q fever.

Three strains of rickettsiae were used—two of these were from ticks found infected in Morocco and the U.S.A. the third was isolated from a patient in Athens. A significant difference was observed between the three strains. The routes of inoculation were intramuscular, intradermal and conjunctival. Some of the infecting suspensions were obtained from the spleens of guinea-pigs, others from ticks (*Rhipicephalus* or *Hyalomma* sp.).

Inoculation by the intramuscular route with spleen substance caused a short spell of fever lasting three to five days, with an incubation period of one or two days. The general symptoms were negligible but the local reaction was pronounced. Rickettsiae could be isolated from the patients' blood.

Tick suspensions inoculated by the same route caused more prolonged fever, often of a two-phase type, but the general symptoms were trivial.

Intradermal injections of spleen substance were employed in ten cases. The only general reaction observed was slight fever in two. The local reaction lasted about ten days and exceptionally there was an exanthematous rash. Rickettsiae could be isolated from the blood in only one of the cases.

Instillation by the nasal route with a few drops of tick suspension was employed in six cases. The only result was a slight rise in temperature.

The only cases in which characteristic pulmonary signs occurred were two in which the patients were caused to inhale heavily infected vapours administered by the aerosol apparatus and a mask. The two operators (though protected by masks) and two other persons who had been present at a distance of several yards, also became infected and developed pulmonary manifestations.

Even the symptomless attacks caused by intradermal inoculation produced a state of immunity.

Rickettsia-agglutination reactions at titres of 1:15 to 1:50 were observed in all the 22 cases in which tests were carried out. (Journ. H. B. M. Soc.)

BILLING, R. & OLLEREN, L. Experimentelle Untersuchungen über die Infektion mit Rickettsia quintana (Jerdon). Experimental Investigation of Infection with *Rickettsia quintana* (Jerdon). Ztschr. f. Hyg. u. Bakt. 1947 Jan. 6 127 No. 1 41-8.

The authors found that suspensions of *R. quintana* in a *Salmonella* suspension caused the usual intracutaneous reaction in rabbits, and that

homologous immune serum prevented the reaction, whereas anti-typhus serum had no inhibiting effect

The homologous immune serum did not kill the rickettsiae, these remained infective to lice after its application

The serum of human convalescents from trench fever also inhibited the *R. quintana* intracutaneous reaction, this observation forms the basis on which a practical test for trench fever can be developed. The serum of persons immunized by trench-fever vaccine had no pronounced inhibiting effect on the reaction

John W D Magaw

BIELING, R & OELRICHS, Lilly Beobachtungen über die Dauer der Infektion mit *Rickettsia quintana* (pediculi) [Observations on the Duration of Infection with *Rickettsia quintana* (pediculi)] *Ztschr f Hyg u Infektionskr* 1947, Jan 6, v 127, Nos 1/2, 49-53

The authors mention that the American Trench Fever Commission appointed during the first world war found that the blood of trench-fever patients might remain infective up to 442 days after the onset of the attack

The present observations were made on Russian prisoners of war employed as "donors" of blood to clean laboratory-bred lice which on several occasions became infected with *Rickettsia quintana* although the prisoners had not been exposed to any risk of infection for two or three years, it was assumed that infection might possibly exist for much longer periods. The infectivity was not associated with recrudescences of the disease in recognizable form, in some cases there were single spells of fever in others there were two or more spells at long intervals, and after these trivial illnesses infectivity to lice might persist for several weeks

John W D Magaw

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## BARTONELLOSIS

RICKETTS, W E Intercurrent Infections of Carrion's Disease observed in Peru *Am J Trop Med* 1948, May, v 28, No 3, 437-51, 6 figs [33 refs]

[A paper of great interest and one to stimulate observation, for the findings are very definite though the number of cases on which they are based is comparatively small.]

Out of 105 cases of Carrion's disease, 50 were attacked by intercurrent infections. Malaria heads the list, as is only natural since the two diseases are endemic in the district where the investigation was carried out. The course of the bartonellosis did not seem to be affected by the malaria though the clinical features of both diseases might be modified. The sweating, splenomegaly and monocytosis present are due to the malaria. When the latter infection occurred in the pre-eruptive stage its course might be very atypical, the characteristic chills and fever might be absent

*Intestinal infections*—including under this heading infections at first systemic, such as enteric fever and others of the group—were most serious. Of four patients with a complicating typhoid fever three died, as did both of two with *Salmonella paratyphi B* infection, three others had what the author calls an "anaerobic intestinal septicæmia", the organism not being identified, and all died. *Entamoeba histolytica* infection is another dangerous complication. The author saw three such and all ended fatally after an acute illness with high fever and symptoms generally like those of the *Salmonella* infection, and at autopsy multiple necrotic septic foci were found in the liver and spleen



*Sciurus nigrum* was found to circulate virus after inoculation with the Azibi and the J Z strains, but not with the O C strain. However, antibodies were developed against all three strains.

The large *Cuniculus paca* was the only species tested which invariably showed circulating virus after inoculation and developed neutralizing antibodies. These last two species also showed most virus in the blood stream, but the amount circulating was far below that appearing in certain infected primates.

Eight species were also tested against the French neurotropic strain but only one, *Nectomys squamipes* was found to be susceptible. E. Huddle

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## DENGUE AND ALLIED FEVERS

MELNICK, J. L. & PAUL, J. R. Experimental Fort Bragg Fever (Pretibial Fever) in Chimpanzees. *Proc Soc Exper Biol & Med* 1948, Mar, v 67, No 3 263-8, 1 fig.

This paper deals with a study of the filtrable virus of the short fever described by DANIELS and GRENNAN and called by them pretibial fever because of the frequent occurrence of a rash on the shins [see this *Bulletin*, 1944, v 41, 278]. An exhaustive investigation by a team of experts failed to disclose the agent.

The virus was later isolated from a patient by TATLOCK, from whose description (*J Clin Investigation* 1947, v 26, 287) the authors quote in stating that it is lethal to hamsters and causes fever in guinea-pigs and rabbits. Tatlock is also quoted as stating that the strain was maintained through 23 serial passages in embryonated eggs and then successfully inoculated into 14 human volunteers, most of whom developed a short spell of fever lasting one or two days, and in "some" of whom there was a pretibial rash.

In the present study the strain of virus employed was received from Tatlock, it was maintained by transmission through hamsters and was found liable to deterioration even when stored at a temperature of  $-70^{\circ}\text{C}$ .

Brain suspensions from infected hamsters, when inoculated into a chimpanzee by combined intracutaneous, subcutaneous, and intramuscular routes, caused a characteristic attack of pretibial fever, the incubation period was 10 days, the fever lasted about two days, there was a raised erythematous patch on the right shin and another on the left forearm, blood taken during the spell of fever and inoculated by the same routes into another chimpanzee gave rise to the formation of neutralizing antibodies, but the animal was refractory and its temperature could not be taken. The first chimpanzee also developed neutralizing antibodies and was found immune when challenged with a further dose of the virus.

Two other chimpanzees developed short febrile attacks after inoculation, and from one of them the virus was transmitted to hamsters by blood inoculation, in both of them, and also in a fifth chimpanzee, whose temperature could not be taken, the presence of antibodies was demonstrated.

Large numbers of hamsters were used for testing the activity of the virus and for the detection of neutralizing antibodies.

Four rhesus monkeys were inoculated with suspensions which were lethal to hamsters but the results were entirely negative.

John W. D. Megaw

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## PLAGUE

MEYER, H. F. & FOSTER, L. E. Measurement of Protective Serum Antibodies in Human Volunteers Inoculated with Plague Prophylactics. Reprinted from *Stanford Med. Bull.* 1948 Feb. v 6 No. 1 75-9

It is not sufficient to establish the bare fact of efficient immunization and the need remains in many infective diseases to determine its degree and duration. Agglutination tests, complement fixation tests and whole blood tests have all proved inadequate. A test known as the mouse protection test is in use now for the measurement of degree of passive immunity in yellow fever typhoid fever and dysentery. The authors apply this to the case of plague and use a subcutaneous infective challenge dose of 2,000 *P. pestis* organisms in 0.2 ml. broth equal to 100 MLD. The test mice were of uniformly susceptible ABC inbred strain and each received 0.5 ml. undiluted immune serum from human volunteers intravenously. The volunteers were separated into 4 groups of 10 each, according to the nature of their prophylactic inoculation. — I. Army prophylactic 3 injections 7 billion formalin-killed. II. Fraction I antigen 2.5 mgm. in 3 doses. III. One injection of 1,000 million avirulent No. 1122. and IV. One injection of 1,000 million avirulent Tjixale. As the differences, first in percentages of mortality and second in the length of survival time are not strikingly significant when considered separately but when the two factors are considered together the results of the test become significant the authors unite the two factors in a protection index the percentage mortality divided by the average time of death.

Conclusions drawn are briefly: — I. Administration of purified fraction I plague antigen (this *Bullet* 1947 v 44 717) to non immune human volunteers results in the production of large quantities of protective antibodies in the blood. Formalin killed virulent plague bacilli and one strain (No. 1122) of living avirulent bacilli are decidedly less effective. The well known strain Tjixale as used in these studies proved non-immunogenic. — Adequate protection requires reinoculation and this stimulates a higher level of antibodies than the primary inoculation, but some individuals fail to react to these "booster" antigenic doses. B. F. Harvey

## CHOLERA

TREK, Ilse. Die Cholera in der Schweiz. Cholera in Switzerland. *Zuch. f. Hig. f. Krankh.* 1947 Jan 6 127 Nos 1-2 166-81 5 cols. (1) is a historical review

RAO, S. R. Role of *Palkis* (Moving Religious Fairs) in the Epidemiology of Cholera with special reference to Sri Eknath Mahara] *Palk India M J Gaz.* 1947 Dec. v 82, No 12, 46-50

Pilgrimages and shrines in India and Arabia have been epidemiologically associated with cholera outbreaks. In the case of the present pilgrimages along a route of over 300 miles travelled on foot, we have an instance of miniature pilgrimage during which a cholera epidemic might have taken place. It is a common custom for palanquin or *palki* carrying the sandals of a saint to be the centre of the procession. Pilgrims start with the *palki* and obtain fresh accoutrements en route. In the same way pilgrims disperse

or arrive back on the return journey Cholera cases may be occurring at the commencement of the journey, may be present in villages on the way, and may be brought back again from the shrine of attendance This pilgrimage started in 1941 "from Patan a town heavily infected with cholera" and came under the author's control only with its arrival within the dominions of the Nizam of Hyderabad He had it under supervision both going and coming within the State and it swelled at one time to as many as 1,500 persons An occasional case of cholera required attention on the outward journey, but in none of the cases did it spread, while on the return of the palki, with nearly 1,100 pilgrims, not a case occurred The precautions adopted were compulsory (indirect) inoculation of all pilgrims, treatment of wells with permanganate or bleaching powder, and great care over the feeding of the pilgrims, which was the obligation of villagers *en route* Inoculation is called compulsory and indirect because no pilgrim was allowed to join who had not been vaccinated It is reasonable to claim that these precautions prevented the outbreak of cholera among the pilgrims themselves and among uninfected villages, through which they passed or to which they gave off their fellow pilgrims

W F Harvey

GOHAR, M A, ELYAN, A, MAKKAWI, M, EISSA, A & BASHATLY, A The Viability of Pathogenic Intestinal Organisms in Sea Water with special reference to *Vibrio cholerae* *J Roy Egyptian Med Ass* 1948, Apr, v 31, No 4, 358-72, 3 maps

It seems certain that all coastal sea water into which local sewage is discharged will be in greater or less degree diluted sewage The viability of an organism like that which is designated the "true" cholera vibrio is important Earlier work, done at a time when selection had not established the definition of the cholera vibrio in its narrowest sense, gives little help in solution of the problem The authors have contributed direct data relating to the recent cholera epidemic in Egypt Samples of water from several Egyptian ports with beach lines on the Mediterranean, the Nile, at the entrance of the Suez Canal and at Suez were artificially contaminated with 5,000 million cholera vibrios per litre and kept at a temperature of about 18°C with the intention of testing them daily for viable cholera organisms The cholera vibrio, however disappeared from all the samples in about 24 hours this could be interpreted as due to the overgrowth of harder organisms or to the presence of an antibacterial substance in sea water The next step was to try the samples out after getting rid of other organisms first by sterilizing, by adjustment of pH, and by making up a synthetic sample of sea water The result of this trial showed that "the life of the organism is very short only in the filtered water which probably contains an anti bacterial agent and is much longer in the autoclaved samples" Filtration was through Seitz filters and autoclaving probably destroyed not only existent organisms but also the hypothetical antibacterial substance Viability of the cholera vibrio was especially long after adjustment of pH to suit its requirements Other experiments were carried out for organisms other than the cholera vibrio and are pertinent to the disposal of sewage generally by discharge into coastal sea water The remarks towards the end of the article sum up the position further — 'From the point of view of bathing and frequenting seaside resorts the danger of discharging sewage into the sea is overestimated The main risk of infection with pathogenic intestinal organisms in the sewage seems to lie not so much in the contamination of the water itself as in the contamination of shell fish' Aesthetic reasons may of course, be an important consideration in a coastal area for the imposition of regulations relating to the discharge of sewage

W F Harvey

BURROWS, W. & HAYES, Isabelle. Studies on Immunity to Asiatic Cholera. V The Absorption of Immune Globulin from the Bowel and its Excretion in the Urine and Faeces of Experimental Animals and Human Volunteers. *J Infect. Dis.* 1948, May-June, v 82, No. 3 231-50 12 figs. [18 refs.]

A preceding study IV has already been abstracted [this *Bulletin* 1948, v 45 135] and indicated that immune coproagglutinin indistinguishable from immune serum globulin was present in the faeces of previously immunized guinea-pigs that had received experimental enteric infection with the cholera vibrio. The present study continues the research into the origin of the faecal antibody whether it might be derived from seepage of serum antibody or direct from antibody-forming cells of the lymph follicles of the intestine the permeability of the intestine to a large globulin molecule and the behaviour of homologous and heterologous globulin in the passively immunized animal. The conclusions to the detailed experimentation are shortly—1 Immune globulin immunologically indistinguishable from serum globulin is excreted in the faeces and urine of actively immunized guinea-pigs and human volunteers. It is independent of serum antibody and therefore is not derived from it. 2 Serum globulin is excreted normally in urine and faeces and immune globulin of immunized guinea-pigs is a partial substitution for normal globulin in the excreta. 3 Antibody appears in the faeces and urine of guinea-pigs passively immunized with homologous or heterologous antiserum. 4 Homologous and heterologous immune globulin administered to the guinea-pigs by intragastric inoculation is absorbed in large amount directly from the bowel without modification of its immunological properties and it is evident that the immune globulin can readily pass in either direction through the bowel wall.

W F Harvey

SARWAT Y. & ADHAM I. Fluid Balance in Cholera. *J Roy Egyptian Med Soc.* 1948, Apr v 31 No. 4 300-303.

Depletion of water and depletion of salt cause the most serious symptoms in cholera. Dehydration requires urgent and immediate treatment but this treatment should be followed by a careful analysis as to how far the alteration in fluid balance is due to pure water depletion or pure salt depletion respectively. Cholera presents a combination of the picture of both pure water and pure salt depletion. As a result of pure water loss, tissue fluid and blood plasma become hypertonic and water is withdrawn from cells. With salt depletion the reverse takes place and tissue fluid becomes hypotonic. As the kidneys excrete water in an endeavour to decrease the clinical picture of salt depletion—thirst, contraction of plasma volume, no reduction of chloride and haemo-concentration, and require water, salt depletion of symptoms balance is—(a) c. of blood above 11 reaction in the later cases.

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intravenous saline, till the specific gravity dropped to 1060, after which it was sufficient to make the patient drink plenty of fluid. As there is usually reduction in the alkali reserve and tendency to acidosis, intravenous 4 per cent sodium bicarbonate is recommended. The work of MARRIOT [this *Bulletin*, 1948, v 45, 208] has greatly clarified the symptomatology of cholera. W F Harvey

SAFWAT, Y & ADHAM, I **Uraemia in Cholera** *J Roy Egyptian Med Ass* 1948, Apr, v 31, No 4, 309-21

A reference is made to the findings of CHATTERJEE and SARKAR [this *Bulletin*, 1941, v 38, 583] which are summarized and which had led those authors to conclude that uraemia in cholera was not due to any structural change in the kidney, but that the cause was extra-renal and pre-renal. Safwat and Adham's own observations tend to confirm this view, and briefly are —(1) Initially all cases had albuminuria which disappeared with recovery of renal excretory function and drop in blood urea, oliguria changed to polyuria, even though blood urea was still high, the specific gravity of the urine was low, and began to rise only when blood urea became normal, casts were sometimes found and a low urinary chloride increased with improvement of the case and with drop in blood urea. (2) Blood uric acid, blood creatinine and blood urea clearance were highly correlated with blood urea values, positively, or negatively. Little evidence was found, from estimation of blood chlorides, of hypochloreaemia. All the results pointed to a marked acidosis initially and gradual attainment of normality with general improvement and with treatment. Clinically the symptoms in cholera were those of dehydration, and symptoms of uraemia were slight even with very high blood urea.

"In other words there was a picture of renal failure developing acutely, coming to a maximum and finally, in the majority of cases, resolving completely in a short time."

Structural changes in the kidney having been excluded as a cause for pre-renal azotaemia there remained the question of the mechanism of the impairment of renal function. Four factors are considered —hypochloreaemia, low blood pressure, disturbance of acid-base balance and nephritis due to toxemia. The first and last of these explanations are rejected and leave the remaining factors as the explanation of symptoms and high blood urea in cholera. W F Harvey

AWNAY, A **Some Haematological Aspects of Cholera Infection** *J Roy Egyptian Med Ass* 1948, Apr, v 31, No 4, 351-7

The author, in Cairo, studied the following haematological aspects of cholera (1) the degree of haemoconcentration, (2) the leucocytic reaction, (3) the erythrocyte sedimentation rate, (4) the erythrocyte fragility.

The degree of haemoconcentration varied widely the specific gravity of the blood was between 1056 and 1078 and the volume of packed red cells was from 48 to 80 per cent, haemoglobin varied from 85 to 135 per cent and the highest figure for red cells was 7,500,000 per cmm. The author found that in almost every case these four data gave a fairly reasonable indication of the degree of haemoconcentration and correlated closely with clinical findings but they had no prognostic significance. The constitution of the plasma also reflected the dehydration in 18 of 25 cases the plasma specific gravity was above 1030 and in 21 of 25 the plasma protein concentration was 8 gm per cent or more.

Leucocytosis of 20,000 to 30,000 per cmm was quite common, and this increase could not be explained solely on the basis of haemoconcentration.

The polymorphonuclear leucocytes were mainly involved and they also showed some left shift. The total leucocyte counts remained high (average about 12,000 per mm<sup>3</sup>) after the acute stage was over and the dehydration had been corrected and even during convalescence. At this last stage eosinophiles characteristically increased and the author suggests that this point should be investigated further.

The erythrocyte sedimentation rate was estimated in 13 cases before and in 11 (after rehydration treatment). The Wintrobe technique was used and corrected by haematocrit readings. Before treatment the corrected E.S.R. range was 0.45 to 1.7 mm/minute (average 0.7 mm.) and after complete rehydration it was 0.6 to 1.5 mm/minute (average 1.0 mm.). The normal reading is 0.1 to 0.3 mm/minute by this method. It is suggested that the higher viscosity of the blood before rehydration interfered with the sedimentation rate. The corrected E.S.R. range in 9 patients during convalescence was 0.3 mm/minute to 0.6 mm/minute (average 0.45 mm.).

The finding of an increased E.S.R. during the acute stage of cholera and for some time afterwards differs from that of the Indian workers (not specified) and the discrepancy is attributed by the author to his having corrected the results by haematocrit readings which he regards as essential.

Increased erythrocyte fragility during the acute stage of the disease was found in 13 of 14 patients when the Sanford technique (diminution, dilutions of NaCl solution) was used and in 6 patients tested by the Wyman method (increasing dilutions of serum with distilled water). In the latter 6 patients, the lysis index was also high (17 to 23 units) in the acute stage but fell to less than 8 units during convalescence. The author discusses the causes of the increased fragility. He believes and quotes experimental evidence to support his belief that in addition to the cholera toxin itself deficient capillary circulation tends to increase red cell fragility. Probably trauma of the cells in marked dehydration and increased blood viscosity may also contribute to the fragility. He suggests that the lysis index is increased as a result of increased phagocytosis of the fragile erythrocytes by reticulo-endothelial cells. This would be favoured by stagnation of blood because of deficient and slow circulation.

H. J. O'D. Burke-Gaffney

EL. RAHUL A. H. Clinical Study of 689 Cases of Cholera Isolated in the Abbassia Fever Hospital. *J. Roy. Egyptian Med. Soc.* 1948, 34, 31-44.  
322-50

It must have been a trying experience for a medical man with no previous experience of cholera to take charge of a large and sudden serious epidemic even though it also made sudden disappearance. Excellent details are given of this epidemic which presents a typical picture of the enteric patient. Diarrhoea, vomiting, and dehydration effects make up the symptoms. The diarrhoea is painless and the vomiting is unaccompanied by nausea. One has always been accustomed to associate colourless rice water stools with cholera and it is interesting to note that the stool is first faecal, becomes colourless and then with the improvement of diarrhoea the stool becomes coloured semi-solid and solid as bile returns. Degree of dehydration as measured by the copper sulphate method for specific gravity of whole blood which ranged from 1.050 to 1.078 in different cases. Blood pressure might be so low that it could not be taken at all or else very low (70 or less) systolic pressure and no measurable diastolic pressure was found. Fever was seldom present and infrequent symptoms were lacerating headache, anuria, and abdominal pain. It was found that the concentration of blood urea, an early feature in cholera, is not related at all to the haemococentration.

Similarly there was seldom any correlation between "blood chlorides and blood urea in the sense that as the blood urea decreased, the chlorides increased". Of complications, high blood urea concentration was the most common. In fact "it should be considered as a symptom and not as a complication" of cholera. Only a minority of these cases showed uraemia and that carried a grave prognosis.

The carrier and contact questions are answered in the data that 50, 91.7 and 100 per cent of carriers were free of vibrios after the first 5, 10 and 15 days respectively. Contacts numbered 2,035 and the number of healthy carriers among them was 84, none of whom showed any signs of gastro-intestinal illness. Cholera rarely developed among contacts. Pathological findings in necropsies and histology are described, and finally treatment is critically considered.—Treatment should be started as early as possible and it must be recognized that "the immediate danger to life is due to dehydration and circulatory failure". It is quite sufficient to give fluids by the mouth in patients with blood specific gravities up to 1060, and 400 ml of normal salt solution should be given intravenously for each degree above that figure, firstly at 2-5 litres an hour and then at a slower rate. Acidosis was combated with "the addition of 40 gm sodium bicarbonate to every litre of normal sodium chloride solution", which was passed through a Seitz filter. Digitalis was the heart stimulant used and sulphonamide drugs produced no effect on the course of the illness or on the case mortality.

*W F Harris,*

carried out on a hospital population, thus restricting it to incidence and fatality in previously vaccinated and non-vaccinated patients. Total admissions to hospital were 430 patients. Out of 281 non vaccinated patients 69 died, while out of 149 vaccinated 14 died—a result in favour of the vaccinated. Other data relate to the decrease in incidence and death rate with the lapse of time following inoculation and to the relative value of a single or a double dose of vaccine. Fatality rate was 9.81 per cent in patients vaccinated with a single dose 8.10 with a double dose and 4.53 per cent in the non-vaccinated. The current question was taken up to determine the duration of excretion of vibrios in convalescent and healthy contact carriers with the finding of a maximum period in the former of 33 days and in the latter of 15 days. One of the conclusions drawn is that vaccination not only afforded "a definite degree of protection but also lowers the fatality rate."

H. F. Harvey

## AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

FULLER E. C. LEWIS Ruth, HEILBRUN Ilse HICAMAN Mary L. M. & EVERITT Martha G. Posibles determinantes de la patogenicidad de la *Entamoeba histolytica*. I. Estudio de sus asociaciones bacterianas y su susceptibilidad a los antibióticos. [Influences determining the Pathogenicity of *Entamoeba histolytica*. I. Study of the Bacterial Associations and their Susceptibility to Antibiotics. *Medicina Mexico* 1948 May 5, v. 28 No. 558, 206-10.]

[This is a translation of a paper delivered at a Medical Congress in Mexico. It deals with a subject of the highest importance. That the growth of *E. histolytica* is influenced by associated organisms is well known and the varied effects of the infection in man may be due to the nature of these organisms. The authors have investigated the bacteria associated with 1 strains of the amoeba, 18 already known, isolated or recorded by Fullin and their fresh strains. In 12 cases the species of bacterium present has been determined, they were mostly Gram-positive cocci and Gram-negative non-pathogenic bacteria of the coliform type. By means of antibiotics penicillin and streptomycin and by sulphadiazine in amounts insufficient to harm the amoeba the organisms were removed from the growths. The resistance of the bacteria varied greatly, some yielded readily, some needed relatively high concentrations, some were quite unaffected. It was observed that the trophozoites might resist the action of high concentration of penicillin and streptomycin for several hours and later develop well in the tubes containing an organism designated T. The early sterility and later development are attributed to late growth of spore-forming bacilli, introduced in the early stage, or secondly to the presence of the antibiotic until diluted sufficiently in the course of experimental re-growing, or thirdly to faulty technique. The first is thought the most probable.]

Tests are to be carried out on susceptible animals with the amoeba and with known isolated bacteria. [The paper contains a table of references made to several tables (cuadros) which have not been included in the present text.]

H. Harold Scott

withstand a concentration of 1/1,000 Soludagenan [ $\alpha$  ( $\beta$ -aminobenzenesulphamido) pyridine] but that the latter behaves in a different manner. The following observations were made in the case of *E. invadens* —

(1) With concentrations of 1/100 to 1/500 there was no growth in the tubes  
(2) In concentrations of 1/600 to 1/2,000, cysts formed from the inoculum, but no trophozoites. Subcultures were negative

(3) In concentrations of 1/2,500 to 1/8,000 some trophozoites and fairly numerous cysts were present after 5 days, but the vegetative forms were not seen after the 10th day, cysts only being present by then. Subcultures were negative

(4) In a concentration of 1/10,000 there were numerous trophozoites and cysts after both 5 and 10 days, but subcultures into a medium containing 1/10,000 of the drug were negative

(5) Below this concentration, both cultures and subcultures were unaffected. Soludagenan therefore exerts a specific action on *E. invadens*, and is the first sulphonamide shown to be an amoebicide. The authors think it probable that other sulphonamides may be found to exert a specific action on *E. histolytica*, in which case their value in treatment would be enhanced as they also act on the accompanying bacterial infection. A R D Adams

EL GHAFAR, Y A. Atebrine in Amoebic Dysentery. *J Roy Egyptian Med Ass* 1948, May, v 31, No 5, 456-60

Twenty patients harbouring vegetative *Entamoeba histolytica* in the stools were treated with atabrine (mepacrine) in varying dosage. Symptoms lessened in a few days and had usually vanished in a week. No parasites (48-hour stool examinations) were seen during, or for 2 weeks after, treatment, except in one case where a few cysts were found. Concurrent infections with *Giardia intestinalis* and *Trichomonas hominis* disappeared with the larger doses of the drug. *Ascaris* ova did not do so. A R D Adams

DURIEUX, C, TRENOUS, J, TANGUY, F, ROBIN, C, RAOULT, A. Recherches sur les propriétés thérapeutiques de la conessine. I. Essais préliminaires dans le traitement du paludisme et de l'amibiase intestinale. L'émétine sera-t-elle détronée par la conessine [DURIEUX, TRENOUS & TANGUY] *Méd Trop* Marseilles 1948, Jan-Feb, v 8, No 1, 7-11. II. Nouveaux essais de traitement de la dysenterie amibienne par le chlorhydrate de conessine [TANGUY, ROBIN & RAOULT] [Studies on the Use of Conessine in the Treatment of Malaria and Amoebic Dysentery] *Ibid* 12-31, 2 coloured graphs

I. In 1935 a study was instituted into the African pharmacopoeia, and of the plants used locally in French West Africa for therapeutic purposes. Among these were specimens of a root, known as "seoulou" and identified as that of *Holarrhena africana*, which is employed for its diuretic and anti-blennorrhagic properties. Analysis showed its composition to be identical with that of Kurchi, *H. antidysenterica* long used in India as an antidysenteric, the active principle of this is conessine, which constitutes about 60 per cent of the total alkaloidal content. *Séoulou* appears to be identical with the "kumbanzo" of Mozambique, which was referred to as a febrifuge by Livingstone in 1856. During the quinine shortage in French W Africa during 1940, the alkaloids of *H. africana* were extracted for investigation of their antimalarial properties. Iodobismuthates of the total alkaloids were not tolerated by the oral route, but on intramuscular

KLATSKIN G & FRIEDMAN H. Emetine Toxicity in Man: Studies on the Nature of Early Toxic Manifestations, their relation to the Dose Level and their Significance in determining Safe Dosage. *Ann Intern. Med.* 1948 May v 28 No. 3 892-915 2 figs. [57 refs.]

Emetine is necessary in the treatment of amoebiasis but fear of toxicity has led to its employment in ineffective dosage. With reasonable care moderate to large doses may safely be given. The early minor manifestations of emetine poisoning in man have received inadequate attention the authors have re-studied these in 93 patients in a U.S. Army hospital. All the patients were confined to bed under close observation during the intoxication particular attention was paid to the blood pressure and the pulse rate and electrocardiogram readings were taken before and during treatment at intervals of three days. The amounts of emetine given ranged from 1 to 27 grains and the drug was given hypodermically intramuscularly or intravenously.

In 91 per cent. of the 93 patients there was some evidence of emetine toxicity the symptoms encountered fell into four categories: local, gastro-intestinal, cardiovascular and neuro-muscular. The side-effects were multiple in 70 per cent. of the patients in 21 per cent. they were limited to one system. The local reaction to the drug was one of the most troublesome it may be less if the injection is subcutaneous rather than intramuscular. Intravenously emetine did not prove more toxic though transient immediate reactions were more frequent. The theoretical objections to intravenous medication are based on the sudden deaths due to ventricular fibrillation which have been seen in experimental animals. Such accidents have not been reported in man but are potential hazards which render routine intravenous therapy unwarrantable. Generalized weakness, electrocardiographic changes and diarrhoea occurred in about half the patients. Signs and symptoms of toxicity in some cases made their appearance after the first dose of emetine but in most they were not manifest until the 10th day of treatment. In a surprisingly high proportion of cases the signs were transient in spite of continued drug administration their severity was usually mild or moderate with little tendency to increase and they rarely continued more than a week after cessation of treatment.

Indications for stopping the drug were precordial pain (in three patients) persistent electrocardiographic changes (in two) neuritis (in four) fainting (in one) nausea and vomiting (in one) and twitching of the muscles and weakness (in one patient).

Emetine "neuritis" was studied, and, in common with similar cases reported in the literature it seemed attributable primarily to a disorder of the muscles rather than to a disturbance of the nervous system. The usual signs of neuritis such as loss of reflexes, changes in sensation and muscular atrophy are usually absent in emetine "neuritis" and the condition is considered to be a toxic myositis rather than a neuritis.

(This paper should be consulted in the original by those interested.)

I. K. D. Adams

LAMY L. & CREVIER A. M. Mille Action comparée d'un amibiocide (le sulfamid) par rapport sur deux amibes parasites. The Comparative Action of Solodagenan on Two Parasitic Amoebae. *Bull. S. Path. Ex.* 1948 v 41 Nos. 3-4 149-53.

In 194 the authors began to study the action of the sulphamide drug on amoebae *in vivo* and *in vitro*. Observations on cultures of *Entamoeba histolytica* and *E. moshkovskii* a parasite of reptiles, show that the former will

withstand a concentration of 1/1,000 Soludagenan [ $\alpha$  (*p*-aminobenzenesulphamido) pyridine] but that the latter behaves in a different manner. The following observations were made in the case of *E. invadens* —

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infection in doses of 0.2 gm. daily into 7 persons suffering from primary benign tertian malaria they were not found to control their infections.

After a study of the literature on hutchinson, a dozen cases of acute or of chronic intestinal amoebiasis were treated during 1941-2 with the hydrochloride of conesine the salts of the secondary alkaloids having been found to cause intolerance when given by the mouth were eventually discarded. The results of oral and of subcutaneous injection having been found similar the drug was usually given in cachets by the mouth in doses up to 0.3 to 0.4 gm. daily to a total of 2.4 gm. over a period of 8 to 10 days. In every case so treated the clinical symptoms rapidly subsided and the stools became normal. One patient relapsed 2 weeks after 0.75 gm. of conesine hydrochloride subcutaneously and 1 gm. of the total alkaloids by mouth retreatment with 0.2 gm. conesine hydrochloride daily for 8 days resulted in [clinical] cure. Another case of chronic amoebiasis previously unsuccessfully treated with emetine acetyltartrate, and other drugs was clinically cured within a week by doses of 0.1 gm. thrice daily. In a third case of double infection with amoebae and with trichomonads both parasites disappeared after a similar course of treatment. Conditions at the time prevented adequate follow-up of the cases to determine if parasitic cure had been obtained, and the investigation had to be abandoned until 1947.

II Between April and September 1947 6 Europeans and 6 Africans suffering from amoebiasis were treated with conesine hydrochloride the clinical effects, the dosage, the therapeutic action, the side effects and the excretion of the drug in these cases were studied in detail. The initial dosage administered is at least 0.3 gm. daily by the mouth for an adult (roughly 0.01 gm. per kilo of body weight over 5 to 6 days) this is decreased during the last day of treatment and the gross dosage administered is 3 to 5.5 gm. There was immediate relief from pain and the disappearance of tenesmus within 48 hours in the acute cases, and the physical signs disappeared, the stools becoming formed and normal in appearance in all of them. In 7 of the 12 cases treated parasites completely disappeared in the others amoebae and cysts persisted. *Trichomonas* infections were cured in a few days. Salvation occurred in two of the European patients. Insomnia appeared early and increased in intensity during treatment it was associated with disturbing dreams and in some cases with disorientation of time and place. Most patients developed headache which became marked and persisted for some days after the completion of treatment. Vertigo and tinnitus occurred in about half the cases.

Conesine caused none of the changes in the urine associated with irritation of or damage to the renal epithelium. It produced a slight but inconsistent diuresis. The urinary excretion of the drug is slow it diuretic action and its excretion through the kidneys are depicted in two graphs.

Conesine compares favourably with emetine in the control of acute amoebic dysentery and can be safely given if the nervous and psychic manifestations attending its use are controlled by the use of one of the barbiturates.

I R D Lums

DARÍ FÁBRICA, R. [Una crítica a la ur de amebiasis intestinal. A Study of the Therapeutics of Intestinal Amoebiasis.] *Rev. A. Hospital Santa Fe* 1947 July-Dec v. 1, Nos. 34-35, 63-70. 30 refs. English summary. A review of the literature and discussion.

WADSWORTH, G. H. The Dysenteries. *M. J. Aust.* 1947 Mar v. 1, No. 3, 15-23, 1 fig.

A general discussion and review.



RODHAIN, J & VAN HOOP M T *Entamoeba knowlesi* n sp, parasite de deux tortues *Terrapina carolinae* et *Platysternum megacephalum* [*Entamoeba knowlesi*, n sp as a Parasite of Two Tortoises] *Ann Parasit Humains et Comparée* 1947 v 22, Nos 3/4, 129-37, 1 fig [12 refs]

BROWN, E H *Giardia Lamblia* The Incidence and Results of Infestation of Children in Residential Nurseries *Arch Dis in Childhood* 1948, June, v 23, No 114, 119-28

The nursery in which this investigation was carried out is one of the largest and most modern in London. The incidence of *Giardia* infestation on admission in children from one to three years was 26.6 per cent and there was no significant difference in the incidence between the age groups.

Direct examination of the stools for *Giardia* cysts is unreliable, and unless repeated examinations are made, a large number will be missed. The ether concentration method consists of the emulsification of a portion of faeces the size of a large pea in normal saline in 1 oz screw-cap bottle, a layer of ether is added and the bottle is then shaken. The lower layer of saline containing cysts and ova is pipetted into a centrifuge tube and spun at 1,500/min for 5-7 minutes. The supernatant fluid is discarded and a loopful of the deposit is placed on a slide with Gram's iodine.

In a group of 86, the incidence in thirty who had previously attended a day or residential nursery was 50 per cent, but that in 56 who had not done so was only 14.3 per cent.

The great majority of the long-stay children over one year old were infested, in one random group the incidence reached 79 per cent, but under the age of one year the incidence was low. There was a rapid rate of infestation after admission. On the other hand the incidence in adults was 3.7 per cent on one examination. There was no significant difference in height and weight between children who had *Giardia* cysts in the stools and those who had not. On admission there was no significant difference between the stools of a *Giardia*-infested child and those of a child not infested.

The inference is that some factors other than *Giardia* must play a part in accounting for the difference between children on admission and those long resident, but no significant difference was found in the haemoglobin levels. There was no evidence of any marked inability on the part of the *Giardia*-infested children to absorb fats.

The group of *Giardia*-infested children treated with mepacrine showed a significantly greater rate of weight gain than the control group and there was a marked decrease in the incidence of loose stools.

The improvement following mepacrine was a gradual process which might be expected to occur in a chronically inflamed intestine, but there appeared to be no definite relationship between the occurrence of *Giardia* infestation and the onset of loose stools. Dietetic upsets, infections of the upper respiratory tract and psychological disturbances are probably the important factors predisposing to the onset of diarrhoea.

The conclusion is that there is no evidence to support the view that severe cases of non-specific enteritis can be attributed to *Giardia intestinalis*. The suddenness of such outbreaks and the rapidity of spread suggests some bacterial or virus cause. [See also this *Bulletin*, 1943, v 40, 54, 699]

P Manson-Bahr

MOHAPATRA, G S *Giardiasis in Children* *Indian Med Gaz* 1948, Jan, v 83, No 1, 14-17

The report is based on 10 cases each of which is described separately. All the patients were children, of whom nine were under the age of 5 years.

Common symptoms were diarrhoea prostration—in proportion to the duration of the infection, although the children usually looked well—flatulence and poor appetite. The tongue was usually clean. Anaemia, in some degree was always noted [no records of blood examinations are given in the case notes so this was presumably a clinical observation]. There were frequent remission of symptoms usually coincident with some form of therapy.

The stools varied in colour and consistency but at some time in each case white fatty stools were passed. In some cases this followed a period of bloody mucous stools. Motile *Giardia intestinalis* were found in large numbers in each case. It was noted that in periods of remission the motility of the flagellates decreased.

Treatment by mepacrine [the author states atabrin or mepacrine] a quarter of a tablet 3 times a day for five days, effected a clinical cure in every case. In two there was a temporary relapse which necessitated a second course. However in all cases the infection persisted for periods up to two months, although the flagellates were reduced in motility. L. E. V. *per*

LIEBOW, A. A., MILLIKEN, T. & HANSEN, Clair A. Isospora Infections in Man. *Am. J. Trop. Med.* 1948, Mar. v. 28, No. 2, 281-73—pla. (44 refs.)

In 1933 MAGATH [this *Bullet.* 1933 v. 32, (60)] summarized all information on this subject and since that time only one external clinical and parasitological study has appeared. This was a survey of German troops evacuated from North Africa by HERRLICH and LIEBOWITZ [ibid. 1944 v. 41, 782].

More than half the previously recorded instances had come from countries bordering the Mediterranean. Additional infections in man have been reported from China, N. and S. Africa, the Philippines, Argentina, Brazil, Russia, Palestine, Japan, Okinawa, Venezuela, Cuba and Mexico and other areas. The present paper deals with patients evacuated from the campaigns in the Pacific. One was apparently infected in the Solomons. Five other soldiers were sent to Saipan from Okinawa.

It is possible that intra-epithelial forms were seen by KJELLBERG and described by VITCHEW as early as 1890. It should be expected that *Isospora* would have an intracellular schizogonic cycle in analogy with other coccidia, but since the instance recorded above only the oocysts and their subsequent transformations leading to the development of four sporozoites in each of two sporocysts are known. GOTO has published evidence suggesting the existence of coccidiosis of the nasopharynx. The oocysts in all the present military patients displayed the typical features of the genus *Isospora*. The length of the freshly passed oocyst at the commencement of segmentation is 31  $\mu$  with a width of 11  $\mu$ .

Development takes place *in vitro* even when the cysts are kept in hygroscopic solutions such as 7 per cent. potassium bichromate or saturated zinc sulphate.

Under condition of room temperature on Saipan the rate is rapid segmentation of the sporoblast. The incidence of infection amongst soldiers evacuated from Okinawa was at least 0.5 per cent and is similar to that of Herrlich and Liebmans series.

Only one of the nine was omitted with actual diarrhoea but they had been a past history in three.

All but one had an eosinophilia of 14 per cent or higher but only the skin worm was also present in four and there is no evidence that this rise of eosinophilia is due to the *Isospora*.

It is probable that signs and symptoms ascribed to infection with this organism are the result of coexistent infection with other organisms. It is

particularly difficult to assess the effect of therapeutic agents since the organisms tend to diminish and ultimately to disappear. There is no dramatic response to mepacrine, quinine, tetrachlorethylene or carbarsone.

An attempt was made to discover where the organisms may occur in the gastrointestinal tract. Miller-Abbott tubes were passed in all five patients and a sigmoidoscopic examination was made in each. Samples of intestinal contents were removed from the duodenum between 8 and 10 inches beyond the ligament of Treitz and at four other levels. Oocysts were found in the aspirated material in two patients.

P Manson-Bahr

MUKHERJEE, N N. Incidence of Coccidiosis in the Arakan. *Indian Med Gaz* 1947, Dec, v 82, No 12, 735-6 [12 refs]

Since the discovery of *Isospora hominis*, some 200 cases of infection by it have been reported, the highest figure in one zone being 32 from the Eastern Mediterranean. The author refers to previous records of cases in East Asia between 1920 and 1936, which varied between one and five in each locality quoted.

In the Arakan, on the Eastern frontier of South Bengal, the present author saw 14 cases of coccidiosis in about 7 months out of some 6,000 stool examinations from over 1,000 soldiers, British and Indian. Twelve of the 14 were detected by direct examination and the other two by Sheather's concentration method (sugar flotation). The findings are summarized in a table. Charcot-Leyden crystals were present in all but two cases. Most of the patients had loose, light-coloured stools with undigested food material. All cases occurred among British troops between May and October, the peak of incidence corresponding with the peak of the monsoon. Nearly all cases originated in the same area, suggesting some endemicity.

The condition was usually mild, and manifested by diarrhoea and some abdominal discomfort, but acute dysentery and prolonged illness of 3 to 5 weeks duration occurred in a few cases. Eight of the patients harboured some associated pathogenic intestinal parasites, such as nematodes or *Trichomonas hominis*.

H J O'D Burke-Gaffney

RENS, M R. *Balantidium coli*. *Nederl Tijdschr v Geneesk* 1948, July 24, v 92 (III) No 30 2225-8, 2 figs on pl.

The English summary appended to the paper is as follows:—

Description of a case of very tenacious and frequent diarrhoea caused by *balantidium coli* a ciliate occurring in the intestine of man, pigs and monkeys. Our case concerned a pork butcher, who, owing to gross uncleanness very likely had infected himself with pigs *balantidia*. Morphology, morbidity, occurrence, reproduction and therapy of *balantidium* are further gone into.

Whereas the very numerous medicaments mentioned in the literature were not or only slightly successful in treating the disease, a speedy and complete recovery was brought about in the case described above by a 10 days' cure of 750 mg enterovioform 'Ciba'."

## RELAPSING FEVER AND OTHER SPIROCHAETOSSES

COLLIER W A. Die Verbreitung der Leptospiren in Niederländisch-Indien [The Distribution of *Leptospirae* in the Dutch East Indies] *Acta Tropica* Basle 1948, v 5, No 2, 135-59.

Eighteen sorts of leptospirae have been isolated in the Dutch East Indies, and serological evidence has been found of the presence of 3 others. Of special

interest is *Leptospira bacteris* which was thought to have a very circumscribed distribution until it was reported from N. Italy (see MINO, *Bulletin J. H. Genev.* 1940 v 13 369).

The nomenclature of these leptospires presents difficulties. On the one hand, the same organism has been given different specific names by different authors while on the other certain workers believe that separation into species is not justifiable. Furthermore such words as type and group are used with a significance different from the meaning accepted in systematics. Collier holds that the antigenic structure of leptospires is constant, and that serological reactions should be used as the basis of classification. The species to which any strain belongs can be determined by agglutination-lysis tests. A species may however contain races which can be separated only by absorption tests. These have been called biotypes in the case of *L. icterohaemorrhagiae* (GISEN & SCHIFFNER, *Zent. f. Bakt. f. Abt. Orig.* 1939 v 144 427) but Collier suggests that they should rank as subspecies or Races—preferably the former. A list is given of the 4 species recognized by the author as being present in South East Asia. Details are set out of each type strain—host, place of isolation and original description—then follow any synonyms, and the distribution of the species in South-East Asia. [The information cannot be summarized.] Subspecies are noted for *L. animalis* (*L. animalis utimulsi* and *L. a. rackmisi*), *L. latitans* (*L. latitans latitans* and *L. b. letali*), *L. icterohaemorrhagiae* (*L. icterohaemorrhagiae icterohaemorrhagiae* and *L. i. neomplesi*). One table shows the areas in South East Asia where human infections with the different species have occurred, another deal with surveys of different animals, and records the numbers tested and the species of leptospires found in the different places.

J. C. BROWN

## NEWS

GOODMAN, L. Sudden Death after Intravenous Sodium Bismuth Tartrate. *Brit. Med. J.* 1943, May 22 978-9.

Previous reports indicate the toxicity of bismuth salts given intravenously and their action on the central nervous system and heart in animals. Despite the very extensive use of bismuth preparation in the treatment of various fatalities have been reported.

Three African women were inadvertently given intravenously 10 grains (650 mgm.) of sodium bismuth tartrate (solbita) in aqueous solution. Two who had received 13 and 10 mgm. of solbita per kgm. body weight collapsed and were dead in minutes. Post mortem examination showed that the only notable abnormality was an unusual flabbiness of the heart. The cause of death was not recognized until the presence of bismuth in the liver was reported. None of the women had contraindications.

The third woman had received 11 mgm. of solbita per kgm. body weight and collapsed 6 minutes later. She was given nuchthamide (1 ml.) and artificial respiration was applied. She recovered consciousness and was given Ardet and intravenous sodium amytal not till 1 hour later but blue line on the gums appeared on the third day. Oliguria started early and resulted in anuria by the fifth day. After intravenous administration of sodium bicarbonate solution no details of dosage are given. Urinary excretion commenced and increased until on the 10th day when death occurred (16 x 450 ml.) was reported. All urine passed after the administration of the solbita contained albumin, red blood specks and 11.4% blood was present (12.2 mgm. per 100 ml. on the last three days). Histological post mortem findings included

a marked blue gingivitis, a litre of clear, pale amber, peritoneal fluid, a soft enlarged liver with recent fibrinous adhesions to adjacent viscera and an inflamed lower colon and rectum with small petechiae. The kidneys were very pale and swollen, with complete destruction of the tubular epithelium and many granular and fatty casts. Kidneys and liver contained much extremely finely divided fat, otherwise the liver tissue showed little change. The relative quantities of bismuth per kgm liver tissue in the three cases were 40, 30 and 23 mgm respectively.

[How three, apparently consecutive, patients were inadvertently given intravenously doses of Sobita of three times the maximum intramuscular dose is not reported. No reference is made to any previous bismuth treatment these women may have received.]

C J Hackett

DOWNING J G Yaws in Massachusetts *New England J of Med* 1948, July 1, v 239 No 1, 17-18 2 figs

Two cases in Negroes who had lived in Jamaica

## LEPROSY

MARTINEZ DOMINGUEZ, V A proposito de la clasificación de la lepra [Proposals for the Classification of Leprosy] *Med Colonial* Madrid 1948 July 1, v 12 No 1 21-49 10 figs

A discussion on existing and proposed classifications

SCHUJMAN, S Tratamiento chaulmoógrico intensivo (intramuscular e intra-dérmico) en los casos lepromatosos no beneficiados con las dosis bajas de la misma medicación. Primeros resultados observados [Treatment of Lepromatous Forms of Leprosy with Large Doses of Chaulmoogra] *Prensa Méd Argentina* 1948, Mar 19, v 35, No 12, 501-5, 3 figs

The author, believing that the poor results of the treatment of leprosy were due to the smallness of the doses generally given, selected 30 patients suffering from the lepromatous form who had been under treatment for many years, some up to 10, on the usual doses of 30-50 cc a month. Of these only five had shown any improvement, 10 had remained stationary and 15 were worse. He started giving them larger doses of 90-150 cc a month. On the whole these doses were well tolerated, the local pain soon passed off and after eight months of this treatment none was worse, one only had remained stationary, 29 had improved, six of them "greatly improved". Photographs show the condition before starting the intensive course and at the end of it, the changes depicted are very marked.

H Harold Scott

FERNANDEZ, J M M & BERGEL, M Recentes investigações sobre o emprêgo metanal-sulfoxilato de sódio no tratamento de lepra [Formaldehyde-sulphoxylate of Sodium in the Treatment of Leprosy] *Hospital* Rio de Janeiro 1948, Apr, v 33, No 4, 549-52 [11 refs]

The authors argued thus for trying this drug. SOULE and MCKINLEY have shown that an atmosphere rich in oxygen affects cultures of [what they thought to be] *Mycobacterium leprae* [see this *Bulletin*, 1933, v 30, 238], GRAU TRIANA has shown the effect exerted by oxidases on such cultures [*ibid* 1945, v 42, 212]. The action of reducing agents on lower, unicellular organisms is different from that on the higher organisms, and therefore it may be possible to disturb [even destroy] the vital function of a pathogenic agent without injuring the body infected by the use of such agents.

Sodium formaldehyde sulphonylate ( $\text{NaHSO}_3 \cdot \text{CH}_2\text{O} \cdot \text{H}_2\text{O}$ ) is a compound of sodium hydrosulphite ( $\text{Na}_2\text{S}_2\text{O}_4$ ) and formaldehyde. The authors prepared a 10 per cent. solution of this drug in doubly distilled water and injected daily 6 gm. (so tated) of it in two doses, intravenously and intramuscularly so as to keep the organism under continuous action of the drug. It was given thus for 10-15 days and renewed after an interval of 5-7 days. Given orally it was badly absorbed and caused diarrhoea. They treated 12 advanced lepromatous patients in this way and report favourably upon the drug—softening and diminution of the lepromata, diminution in numbers and staining properties of the bacteria. Later to assist the reducing action they gave ascorbic acid also but the results were no better in fact some seemed to recede. It is thought that in spite of the reducing action the ascorbic acid may in some way interfere with that of the metanal and sulphonylate.

Three hypotheses are put forward regarding the beneficial action of the drug. (1) That it is not specific but is merely a reducing agent. (2) That it acts as a specific poison in a certain stage of "wide reduction" (the *M. o. leprae*). (3) That it acts as a poison on [presumably in] fishes with] some essential metabolism required by the organism. The authors hope to carry out more tests on a larger scale.

H. Harold Smith

SCHOLTER C. Tierexperimentelle Studie zur Chemotherapie der Lepra. (Animal Experimental Studies on the Chemotherapy of Leprosy) *Zuckerf. Hyg. Infektionskr.* 1944 Nov 12, v 124, n 1/2, 1-6

## HELMINTHIASIS

GAUD J & MAIRICE, A. Foyers de bilharziose fécale dans le Soud. (Foci of Urinary Schistosomiasis in the Soud Region.) *Bull. Inst. Hyg. Maroc* 1946 6 61-2

The existence of urinary schistosomiasis in the Wady Sous region of Morocco is confirmed. In three foci (Km. 44 Ut Baha and Tanalt) the infestation rates in children in July 1947 were respectively 10, 9 and 86 per cent. The incidence seemed to be greater in the mountain (Anti Atlas) than in the plain. Malacological investigations were negative.

H. J. O'D. Burke-Gaffney

CRAW ELOISE B. [Studies on Schistosomiasis. Objectives of Research, Sources of Material, and General Methods. *Nat. Inst. Health Bull. No 163* Wash. 1947 49-54

The maintenance of a steady supply of material for schistosomiasis research in the United States was an essential part of a project designed primarily for the needs of the military forces and secondarily for the long range concerns of public health. The principal sources of material as listed supplies of eggs of *S. mansoni* were furnished for over 3 1/2 years from leishman monkey which had been experimentally infected. Eggs of *S. haematium* were obtained from a hamster experimentally infected and from a fat tailed gerbil, *Meriones libani* was also experimentally infected. Eggs of *S. japonicum* were supplied by a Philippine dog. Snail intermediaries were shipped from various sources either as adults or eggs.

The methods of shipment of snails eggs and subsequent treatment and the general methods employed in the laboratory for collecting schistosomes from and exposing snails to infection are described.

J. J. C. Buckley

LEIST, W H The Geographical Distribution and Molluscan Intermediate Hosts of the Schistosomes maturing in Man. Nat Inst Health Bull No 139 Wash. 1947, 1-45 [204 refs]

In this compilation "the schistosomes maturing in man" are restricted to the three well-known species *S. haematobium*, *S. mansoni* and *S. japonicum*, and the author reviews critically the current position with regard to the validity and status of other less well-known or controversial species reported from human hosts. Doubtful or questionable distribution records of the three main species are discussed and considerable effort has been made to produce a complete and authentic list of localities.

The names of molluscan intermediaries are listed with the localities, together with annotations relating to their nomenclature, and status as authentic or merely inferential hosts. The list of 201 references is classified under geographical headings. J J C Buckley

BERRY, E G Snails collected for the Schistosomiasis Investigations Nat Inst Health Bull No 189 Wash. 1947, 55-69, 1 fig on pl.

Collections of snails for schistosomiasis research in the United States were made by the author from 11 States: Michigan, Kentucky, North Carolina, South Carolina, Georgia, Florida, Mississippi, Louisiana, Texas, Utah and California. Particular attention was given to the collection of members of the family Amnicolidae, of which the genus *Oncomelania* is a member.

From more than 150 localities in these States, 54 species of Amnicolidae, Pomatiopsidae and Planorbidae (including the genus *Tropicorbis*) were taken. The species in this collection are listed together with those of another collection. In all, 103 species and sub-species were identified, representing nine families of molluscs. J J C Buckley

GRAM, Eloise B, FILES, Virginia S & JONES, Myrna F Experimental Molluscan Infection with *Schistosoma mansoni* and *Schistosoma haematobium* Nat Inst Health Bull No 189 Wash. 1947, 81-94 [25 refs]

The authors exposed 23 species and subspecies of native American snails the family Planorbidae and 4 species of non-planorbids to infection with the Puerto Rican strain of *Schistosoma mansoni*. The only susceptible species was found to be *Tropicorbis havanensis* (Pfeiffer), which produced cercariae infective to mice. Exposure of American snails to infection with *S. haematobium* gave negative results but the authors comment upon their lack of success in infecting *Bulinus contortus* and *Physopsis africana* with *S. haematobium*. J J C Buckley

GELFAND, M Bilharzial Affection of the Ureter A Study of 110 Cases of Necropsies showing Vesical Bilharziasis Brit Med J 1948, 1, 1228-30 [10 refs]

The ureter is often affected in bilharziasis. In 110 consecutive post-mortem examinations in Salisbury, Southern Rhodesia, on adult Africans from an endemic bilharziasis area, ureteral dilatation was found in 25 cases, three had ureteral strictures. In 16 of the 25 the dilatation was unilateral [below], in 6 of these it affected the whole length of the ureter, in 5 the dilatation was unilateral (sic), [? bilateral], in 2 of these the whole of the ureter was involved, in 4 the middle third, and in 3 the middle third.

The diseased portions of the ureter are readily identifiable by changes in their colour, texture and appearance. These were usually found in the lower third. Too dilatation occurred in the absence of such changes. If the cause of the dilatation were stenosis it would be expected that the whole of the ureter above the constriction would be dilated, and the dilatation would not be confined to the site of the disease as was found to be the case. The dilatation is therefore directly attributable to damage to the ureteral wall by the disease. The disease is thus associated with ureteral dilatation but rarely with stenosis as has previously been thought. The dilatation and thickening of the ureteral wall lead to impaired peristalsis with stasis, and possibly reflux of urine from the bladder. These in turn cause hydronephrosis.

Eight cases of hydronephrosis were encountered, and 4 of these in which the condition was bilateral showed ureteral dilatation. One case of these four was attributable to a congenital abnormality of the urteric openings in the bladder. In one case of ureteral stenosis there was hydronephrosis on the same side as the stricture. In 2 of the 3 cases with ureteral stenosis there was no hydronephrosis. Three cases of carcinoma of the bladder were associated with bilateral hydronephrosis, due to lower ureteral obstruction by the growths.

Histological sections of the bilharzial disease in the ureters showed ova to be present in the submucosa and between the muscle bundles in the muscular layer. Tubercle formation so common in the appendix, was not seen. The separation of the muscle fibres results in their atrophy, and the affected portion of ureter becomes dilated, elongated and tortuous. The changes in the ureteric orifices in the bladder were inconstant but in no case was there true stenosis with occlusion.

J. R. D. Adams

IBRAHIM, M. SOLEH A. & EL-SHAHAF A. The Role of Urinary Bilharziasis in the Production of Hypertension and Cardiac Decompensation. *J. Adv. Egyptian Med.* 1st 1948 May v 31 No 5 444-62. (10 refs.)

The authors review their findings in 89 cases of hypertension (57 essential and 32 nephritic). Four (7 per cent.) of the cases of essential hypertension had associated urinary bilharziasis. 13 (40.8 per cent.) of those with renal hypertension had evidence of the disease. 8 (18.7 per cent.) other cases were considered probably to be of bilharzial origin. Secondary infection of the kidneys following a urinary bilharzial infection leads to renal hypertension if this is due to a one-sided lesion nephrectomy may be considered.

J. R. D. Adams

CRAM, ELOISE B. & FILES, VIRGINIA S. Experimental Mammalian Infection with the Schistosomes of Man. I. Laboratory Animals as Source of Supply of Adult Schistosomes and their Ova. *Nat. Inst. Health Bull.* No. 189 Wash. 1947 101-5

Attempts to establish and maintain the three species of schistosomes of man in laboratory animals were successful in the case of *S. mansoni* and *S. japonicum* but not with *S. haematobium*. Monkeys were infected with cercariae of *S. mansoni* from Austral & glabra by the method which are described but their relative effectiveness could not be determined. Subcutaneous injection of *S. mansoni* cercariae into dogs, goats, cats, guinea pigs, and various trials with smaller laboratory animals it was concluded that the best results derived from intraperitoneal injection of mice and hamsters. Dogs were found to be excellent hosts for *S. japonicum* and golden hamsters and white mice were also of value for them. In flea & tick infections of the latter animals the mortality was high in the prepatent period. J. J. C. Finkler



CRAM, Eloise B & FIGGAT, W B **Experimental Mammalian Infection with the Schistosomes of Man II Comparative Study of *Schistosoma mansoni* and *Schistosoma japonicum* Infections produced by Immersion and by Intraperitoneal Injection** *Nat Inst Health Bull No 189* Wash 1947, 106-8

Hamsters were exposed to infections either by immersion or by injection with known numbers of cercariae, in two experiments in which *S. mansoni* and *S. japonicum* were used respectively. With *S. japonicum*, 49 per cent of the cercariae developed as the result of the immersion method and 51 per cent by the injection method. With *S. mansoni* 33 per cent of the cercariae developed from the immersion method and 19 per cent from the injection method.

J J C Buckley

OTTOLINA, C **El problema clinico de la Schistosomiasis Mansoní ante nuevos metodos diagnosticos y sus resultados [New Diagnostic Methods for Schistosomiasis Mansoní]** *Medicina Mexico* 1947, Dec 25, v 27, No 546, 553-64 [27 refs]

The author in dealing with this clinical problem offers a few remarks on treatment, but these contain nothing new and the main part of the paper is on the question of diagnosis. He quotes various reports showing that examination of the faeces yields but a comparatively small proportion of patients actually infested, from 2 to 9 per cent. Rectal biopsy, however, demonstrates some 20 per cent. Even when the ova are present in the rectal tissues in large numbers ("many thousands" says the author) they may not pass into the lumen and so not appear in the faeces, in short, the absence of ova in the faeces is no proof that *Schistosoma* infestation does not exist. Even a positive rectal biopsy does not prove active disease unless the ovum seen contains a living miracidium. Another advantage of the method is the diagnosis of latent or asymptomatic schistosomiasis and of extinct infestation. Cases, he states, may be divided into four groups: (1) *True latent infestations*, the worms being alive and the ova some living, some dead, but there are no clinical signs or symptoms. (2) *Latent extinct*, the worms have died recently and a few living ova may still be present, again without symptoms. (3) *Active disease*, live worms, live eggs and symptoms present. (4) *Extinct infestation*, worms dead and no live ova seen even after repeated examination.

H Harold Scott

WARD, P A, TRAVIS, Dorothy & RUE, Ruth E **Methods of establishing and maintaining Snails in the Laboratory** *Nat Inst Health Bull No 189* Wash 1947, 70-80, 2 figs

The methods employed in maintaining in aquaria amnicolid snails known to serve as intermediaries for *S. japonicum*, are described in detail, together with observations on their breeding habits in the laboratory. *Oncomelania quadrasi* bred satisfactorily in the conditions described but the propagation of *O. nosophora* and *O. hupensis* was more limited.

J J C Buckley

WARD, P A, TRAVIS, Dorothy & RUE, Ruth E **Experimental Molluscan Infection with *Schistosoma japonicum*** *Nat Inst Health Bull No 189* Wash 1947, 95-100

Twelve species of American snails, of the family Amnicolidae, were exposed to infection with *Schistosoma japonicum* in 1945, and five species of Amnicolidae and Pomatiopsidae in 1946. One species, *Littoridina monroensis*, proved to be particularly attractive to miracidia, but failed to develop sporocysts. Of 286

specimens of the species *Platyschistosomum lapidarium* which were exposed, developed sporocysts resembling those of *S. japonicum* but this result is regarded as inconclusive. Control experiments with *Oncomelania nasopharyngis* generally produced positive results.

J J C Buckley

JONES, Myrna F & BRADY F J. Survival of *Schistosoma japonicum* Cercariae at various Temperatures in several Types of Water. *Nat. Inst. Health Bull* No. 189 Wash. 1947 131 & 1 fig.

The authors noted experimentally the following death points for cercariae of *S. japonicum*: 4 hours at 40°C, 20 minutes at 45°C, 3 minutes at 50°C, and one minute at 55°C. With cercariae of *S. mansoni* the results were 20 minutes at 45°C, 2 minutes at 50°C, and 1 minute at 55°C.

Within the range 15°C to 40°C, the survival of the cercariae of *S. japonicum* decreased as follows: At 5°C, a few survived 8½ but none survived 10½ days; at 10°C, some survived 4½ but none survived 6½ days; at 20°C, and 25°C, some survived 2 days, but none survived 3 days; at 30°C the maximum survival observed was 22 hours; at 40°C, some survived 3 hours but none survived 4 hours.

The survival of cercariae at temperatures ranging from 5°C. to 35°C. in a variety of waters was also tested, namely: ammonia free distilled water buffered at pH 7.0 to 7.1; a slightly alkaline raw surface water obtained from a filter plant; a more alkaline water from a pool containing dead leaves and their plant debris; a raw water acidified by contact with peat moss; and water from aquaria in which stock snails, *Oncomelania quadrata* were living. The pH of the more acid water was 5.5 to 6.5 and that of the other raw waters 7.2 to 8.4. It was found that the survival of the cercariae at each temperature was the same in all the raw waters irrespective of different pH values. Their survival in buffered distilled water at 30°C. and 35°C. was the same as in the raw waters but was less at 5°C. and rather longer at 35°C.

J J C Buckley

BOZICAVICH J & HOVEM, Helen M. Intradermal and Serological Tests in Patients with *Schistosomiasis Japonica*. *Nat. Inst. Health Bull* No. 189 Wash. 1947 199-212.

Intradermal and complement fixation tests were conducted on a group of 474 patients demonstrated to have or to have had *Schistosomiasis japonica*. The antigens were prepared from cercariae and adults of *S. mansoni*. Intradermal tests with an antigen prepared from cercariae gave fewer falsely positive reactions with unexposed control individuals than did antigen prepared from adult worms. The use of adult worm antigen resulted in a higher percentage of positive intradermal reactions than did the cercarial antigen. The complement fixation test gave a higher percentage of positive reactions than did the intradermal test. The optimal dilution of the cercarial antigen could not be determined because of insufficient material.

"The results of both the intradermal and complement fixation test gave better correlation with results of the stool examination conducted in the United States than they did with those conducted overseas. Early infection may be the factor which would explain the discrepancy in these results.

"Because of the conditions under which this investigation was conducted, the immunological findings probably be less reliable than did the stool examinations in the diagnosis of the disease.

"For this reason improvement will have to be effected in immunological methods before such tests can be reliably employed in diagnosis."

JONES, Myrna F, NEWTON, W L, WEIBEL, S R, WARREN, H B, STEINLE, Mary L & FIGGAT, W B The Effects of Sewage Treatment Processes on the Ova and Miracidia of *Schistosoma japonicum* Nat Inst Health Bull No 189 Wash 1947, 137-72, 1 fig

The sewage treatment processes which are considered in this report in relation to their effect in destroying schistosome eggs and miracidia or in relation to their effect in concentrating eggs and miracidia in streams which might contain potential snail hosts, include the following Primary sedimentation, anaerobic digestion of sludge, air drying of sludge, the activated sludge process, filtration with a trickler filter, and intermittent sand filtration After a discussion of sewage and sewage treatment generally, with special emphasis on the processes concerned in the investigation, the technique and procedures employed in testing their effect on eggs of *S japonicum* are described in detail

*Primary Sedimentation*—From tests carried out in a 19-inch column of sewage it was found that quiescent sedimentation for 5 minutes removed 25 per cent of the eggs, 10 minutes, 47 per cent, 30 minutes, 80 per cent, 1 hour, 97 per cent, and two hours, 98 per cent The settling rate was estimated as varying between 0.33 and 1.4 inches per minute Although some eggs could escape with the effluent in primary tanks, it is concluded that the majority would be removed by primary sedimentation during the normal detention period

It was found that raw and institutional sewage would not permit hatching in 24 hours but did not destroy the eggs in this time In a dilution of one part of raw sewage to three parts of water, or one part of settled sewage to two of water the eggs would hatch

*Anaerobic sludge digestion*—Experiments were set up to determine how long the eggs could survive in the sludge digestion sections during this process At 75° to 85°F during the first week, about  $\frac{1}{4}$  of the eggs were rendered incapable of hatching This reduction continued during the second week and was greatest in the third week and there was no hatching on the 24th day of digestion It is believed, however, that the temperature and time factors played a large part in this reduction in the viability of the eggs

*Sludge drying*—In drying digested sludge many eggs were mixed and allowed to dry for varying periods It was found that the retention time on the drying bed was more closely related to destruction of the eggs than was the moisture content, so long as the latter was 40 per cent or over Thus, sludge which is to be dried to 60 or 70 per cent moisture content before disposal would need to be retained for 3 weeks to ensure the destruction of any eggs which might be present

*Trickling filter treatment*—This secondary treatment of the effluent from primary sedimentation tanks which sometimes may carry over with it schistosome eggs, was tested in relation to its effect on the eggs It was found that filtration reduced the number of eggs but in all experiments some got through Secondary settling of the effluent reduced these but failed to remove them entirely In such conditions additional treatment such as chlorination is indicated

*Activated sludge*—Experiments were set up to determine the survival of schistosome eggs in activated sludge Hatching of most of the eggs occurred in the first 24 hours and very few miracidia were recovered after 3 days, indicating that the activated sludge is an excellent hatching medium A post-treatment process designed to destroy or remove miracidia is again indicated.

*Intermittent sand filtration*—In five experiments, employing this process, in which the rate was 100,000 gallons per acre, per day, sand with an effective size of 0.3 mm and a uniformity coefficient of 2.6 being used, it was demonstrated to be an efficient method of removing eggs of *S japonicum* from sewage



*Aerosol OT (dioctyl sodium sulphosuccinate)* —The tests showed that only in relatively concentrated solutions was this compound effective but that in non-lethal concentrations it might enhance or accelerate the effects of other cercaricides

*Copper sulphate* —Tested in concentrations of 5, 10 and 50 p p m, it proved effective only at 50 p p m, or more. It could not be relied upon at 5 or 10 p p m to kill cercariae within a reasonable time

*DDT in emulsion with Triton and xylene* —In limited tests this proved to be not an effective cercaricide in concentrations of 0.05 and 0.1 p p m, but at 10 p p m killed cercariae within 75 minutes

J J C Buckley

JONES, Myrna F & HUMMEL, Mirtiel S. The Effect of Chlorine and Chloramine on Schistosome Ova and Miracidia. *Nat Inst Health Bull No 189* Wash 1947, 173-9

"Hatched miracidia of *S. japonicum* were killed within 30 minutes after chlorination with total 30-minute residuals of 0.2 and 0.4 p p m. Similarly, they were killed in chloramine solutions with 30-minute chloramine residuals of 0.3 and 0.4 p p m. *S. mansoni* miracidia were killed within 30 minutes after chlorination which resulted in total residuals at 30 minutes varying from 0.2 p p m to 0.6 p p m and less than 0.1 p p m free chlorine present.

"Ova of *S. japonicum* are more resistant to chlorination than are miracidia. Ova were consistently killed within 30 minutes only in tests in which the 30-minute total residuals varied from 3.9 to 11 p p m. A few ova survived 2-hour treatment with chlorine and chloramine concentrations of 1.52 and 1.65 p p m and 30-minute residuals of 0.75 and 1.1 p p m respectively. No ova survived in one test after an applied chloramine concentration of 1.9 p p m and a 2-hour chloramine residual of 0.5 p p m. Ova were killed in tests with an applied chlorine of approximately 2 p p m and 2-hours residuals varying from 0.7 to 1.4 p p m."

NOLAN, M O, MANN, Elizabeth R & CHURCHILL, Helen M. The Protective Value of Chemically Impregnated Fabrics against Penetration of Schistosome Cercariae. *Nat Inst Health Bull No 189* Wash 1947, 180-98, 1 fig

Standard army uniform materials were used in tests to determine the relative value of chemically treated fabrics as a means of protection against the penetration of schistosome cercariae. Seventy-five chemical compounds, including combinations of chemicals and emulsions, were used to impregnate fabrics and were tested for toxicity to cercariae. The tests were conducted at intervals after repeated rinses of the treated fabrics in water. Mouse exposure tests were subsequently conducted to determine the protective value of those chemicals that in the preliminary tests were most effective against cercariae and most resistant to water rinses. More than 2,000 mice were exposed to cercariae in the testing of 18 chemical compounds and emulsions used to impregnate cotton herringbone twill fatigue uniform cloth, khaki cotton uniform twill and khaki woolen serge cloth. Since water solubility of the impregnated compounds was an important factor, the majority of the mouse exposure tests were conducted at intervals after repeated rinses of the fabrics in water. Fabrics impregnated with emulsions of the cercaricides were also tested for resistance to mild laundering with soap.

The most effective chemical was N,N-diethylauramide which protected mice against penetration of *S. mansoni* cercariae through at least 144 hours of rinse and afforded considerable protection even after 180 hours of rinse. The emulsion of the compound, however, was one of the least resistant to washes

with soap. The compound in acetone solution appeared to be more resistant to soapy washes than the emulsion of the compound.

"Dibutyl phthalate was somewhat less effective but provided protection for more than 96 hours of rinse. The emulsion of the compound was more resistant to soapy washes than was *N,N*-diethylauramide emulsion since it lasted through five washes.

Tests with *S. japonicum* cercariae were less numerous than those with *S. marginata*. However it would appear that the two species reacted in the same manner to treated fabrics.

A measure of protection was afforded by the untreated materials. "Woolen serge cloth in particular was a good mechanical barrier."

McMULLEN D. B. & BRACKETT S. Studies of Schistosoma Dermatitis. X. Distribution and Epidemiology in Michigan. *Amer J Hyg* 1948, May v 47 No 3 259-70 2 figs.

In a survey of schistosoma dermatitis in Michigan, 510 beaches on 177 lakes have been examined. Of these, 351 were found to have populations of carrier snails. On 130 beaches it was possible to demonstrate the presence of the infections in the snails collected. In others, infections undoubtedly could have been found at certain times of the year when adult snails were present.

"The distribution of *S. marginata* has been thoroughly investigated. It is most common in the northwest part of the Lower Peninsula and in the eastern section of the Upper Peninsula, and it is the most important vector for water itch in Michigan. In a few areas *Physa* spp. have been shown to be the cause of outbreaks and in 3 or 4 lakes *L. stagnalis* was suspected of being the source of the trouble. In all of the beaches examined the 3 snails, *S. marginata*, *Physa* spp. and *L. stagnalis* appear in the ratio of "1 ~ 1" and the ratio of the infected snails was found to be 39 : 3 : 1. These ratios indicate quite well the relative importance of the 3 snails in the water-itch problem in Michigan. Water itch is found primarily in the northern part of the Lower Peninsula and the eastern portion of the Upper Peninsula. This coincides with the density of the *S. marginata* populations. The sporadic cases that appear in other parts of the state apparently are caused by schistosoma cercariae coming from *L. stagnalis* spp. and *L. stagnalis*.

VON BOASDOFF D. Pernicious Anemia caused by *Diphyllobothrium latum*, in the Light of Recent Investigations. *Blood* 1948, Jan., v 3, No. 1 91-102. [29 refs.]

In Finland infestation with the fish tape worm, *Diphyllobothrium latum*, is extremely common, in certain Provinces more than 90 per cent of the population being infested. In most carriers the worm is a relatively innocent parasite but in some it causes a macrocytic anaemia resembling pernicious anaemia although differing in its age incidence, the absence of achlorhydria in many cases and the absence of neurological content. That the anaemia is due to the worm seems proven by the fact that the anaemia undergoes complete remission after the worm is expelled, without any further need for ant-anaemic treatment. There seems no doubt that the worm contains a powerful toxin, and theories to explain the anaemia have included arising permeability of the intestinal wall to worm toxin, individual susceptibility of the haemopoietic system to the toxin or an allergic factor. Complete recovery from the anaemia after the worm has been expelled implies that there is no lack of haemopoietic principle. Experiments have shown that the gastric juices of patients with fish tape worms contain intrinsic factor and the anaemia may occur even though the food

contains extrinsic factor, although a relative deficiency of extrinsic factor may aggravate the disease. The clinical picture gives no reason to believe that absorption is impaired, carriers of the worm seldom suffer from intestinal disturbances and glucose tolerance tests showed no deviation from the normal. Powdered worm mixed with gastric juice, meat or hog's stomach failed to destroy the anti-anaemic action of these preparations in pernicious anaemia. It is suggested that possibly any inhibition of interaction between intrinsic and extrinsic factors can only be produced by the living worm in its natural surroundings at the place where interaction occurs. By intestinal intubation and examination of aspirated material for eggs, evidence was obtained that with anaemia the worm is found higher up in the intestine than when anaemia is absent, and it is suggested that in the higher regions, the worm interferes more with the interaction between extrinsic and intrinsic factor, the border zone lies 140 to 150 cm from the mouth, namely about the junction of the jejunum and ileum [See also this *Bulletin*, 1948, v 45, 97, 198, 260]

F Murgatroyd

LE GAC, P. Toxicité des sels d'étain vis-à-vis des plathelminthes [Toxicity of Salts of Tin to Tapeworms] *Bull Soc Path Exot* 1947, v 40, Nos 11/12, 452-5

The author presents observations on several cases of Taeniasis which were successfully treated with stannous oxide (Stannoxy)l. He gave 6 to 8 tablets daily and the worms were expelled in 2 to 6 days. The author also mentions a proprietary vermifuge prepared from salts of tin and metallic tin which gave similar results. The preparation is sold under the name of "Taenifuge Ercé" (Laboratoires Rabent et Carrière). It is stated to be absolutely harmless and keeps well for long periods in the tropics. In a discussion, MONTEL confirmed successes with Stannoxy, which he gave in doses of 18 tablets daily (6 morning, noon and evening). No purgative, special regime or bed rest was required.

H J O'D Burke-Gaffney

WILLIAMS A A. Cysticercosis Cerebri mistaken for Cerebral Syphilis. Report of a Case. *Lancet* 1948, July 24, 144

THIODET J. Manifestation rétrograde de la réaction de Casoni [A Late Manifestation of the Casoni Reaction] *Bull et Mém Soc Méd Hôpît de Paris* 1947, Nos 19/20 467-8

STOLL N R. El problema de la investigación de la uncinaria [The Investigation of Hookworm Disease] *Medicina Mexico* 1948, May 25 v 28, No 556, 197-206

A review of methods used

TINER J D & CHIN T H. The Occurrence of *Ascaris lumbricoides* L 1758 in the Muskrat, *Ondatra zibethica* L [Research Notes] *J Parasitology* 1948 June v 34 No 3 253

BALDWIN, E. A Study of Anthelmintic Potency in relation to Chemical Constitution. *Brit J Pharmacol & Chemotherapy* 1948, June, v 3, No 2, 91-107 [30 refs]

The author tested 200 chemical compounds for detection of anthelmintic potency. Pig *Ascaris* was the test helminth used, and it is claimed that, while

the technique used has certain limitations, it is important that experimental material of nematode origin should be the basis of methods of this kind.

The results are discussed in great technical detail and should be studied in the original but they were at variance with those of earlier investigators in most respects, especially in respect of lactones. More than 30 types of lactones were tested by the author but not one showed activity comparable with or even approaching that of santonin (itself a lactone). This contrast with the findings of other workers is attributed by the author to the use of different "two methods" many of the observations reported in the literature have been prejudiced, in the author's opinion by the use of anelid material.

H J O'D Burke-Gaffney

DE RYKES PUGNAIRE, M. Tratamiento de la elefantiasis de los miembros inferiores. (Treatment of Elephantiasis of the Legs.) *Med. Cosm.* Madrid. 1948, June 1 v 11 No. 6 441-63 13 figs. [75 refs.]

The author reviews the various methods of treatment of elephantiasis of the legs, referring first to medical treatment, later and in more detail to surgical measures. He mentions first antistreptococcus serum and states that he has obtained good results if there is inflammation present with vaccines he reports very good results especially in accessions of elephantoid fever. He quotes records of others such as autobaemotherapy, gentian violet, fibrolysin, iodides, sulphonamides in the fever but makes no mention of having tried these on his own patients and notes that in most cases any benefit had been only temporary. During attacks of fever he employs at the same time sulphonamides, local warmth and an ointment of ichthyol 15 gm., Tr. fodi 15 gm., camphorated oil 30 gm. with compressing bandages.

He then passes on to describe operative treatment in particular detail Hondoleon's operation and modifications of it. He sketches the history of operative measures and then gives a fuller account of his modification (the operation with illustrations to indicate the steps, and photographs showing the intermediate and final results. He removes the fascia and poneurus of the legs and the dorsum of the foot with extensive dissection. In some cases a second and even a third operation are needed, but the results as depicted are in some cases at least remarkably good. After the operation he dusts with sulphonamid powder then stitches the skin without any drainage. He quotes records from the Mayo clinic giving a mortality of 4.7 per cent., and "satisfactory results" in 62 per cent.

The author gives a table of 7 patients under his care the methods of treatment are stated, but not the results. Of the total, 14 were treated medically and 33 had some operation, 10 the P. yr Hondoleon's stretch, 20 the author's method with previous resection of the muscle fascia three had, in addition to this on account of chronic ulcer a preliminary lumbar sympathectomy, 10 had extensive removal of tissue on both the front and back of the leg. He concludes that medical treatment is of much importance as an adjunct and as preparatory to surgical measures.

H Harold Smith

MAZZOTTI, L. Observaciones sobre la oncocerciasis en Mexico. (Observations on Onchocerciasis in Mexico.) *Med. en Mexico* 1948 June 10 v 28, No. 557 17-24. 18 refs.

Onchocerciasis prevails in Mexico at heights of 400-1,300 metres above sea-level and chiefly in the States of Chiapas and Oaxaca, which are sub-tropical with a less than rainfall. The vector are *Simulium ochrocephalum* and *S. metallicum* especially the first which breeds in small collections of water moving slowly the two other prefer larger collections moving rapidly.



In man the nodules are often in the head, less often in the thorax and lumbar region, and usually up to six in number, but they may be many more. In 34 patients, 325 biopsies were performed. 52 per cent of nodules were on the face (or head), 65 on the shoulder, 52 on the forearm, 39 on the hand, 44 on the thorax, 34 on the thigh and 16 on the foot. From one patient with a thigh nodule an inguinal [? femoral] gland was extirpated and 11 microfilariae were expressed from it. The skin may become of a dark greenish colour, in fact, it is known in Mexico as "mal morado" (purple disease). Sometimes allergic attacks occur with fever and local induration so that in time the skin becomes thick and hard, "woody", these attacks are known in Guatemala as "Coast erysipelas".

Treatment is by Hetrazan, which is 1-diethylcarbonyl-4-methyl piperazine hydrochloride, in doses of 2 mgm per kilo body weight, once on the first day, twice on the second, and thereafter three times daily for 3 weeks or more. Some of the author's patients took it for 6½ weeks, but, as tested by biopsy, the results after the longer course "were not appreciably better than after the shorter" [See also this *Bulletin*, 1948, v 45, 532, 533] H Harold Scott

JEFFERY, G & OLIVER-GONZALEZ J  
Puerto Rico [Research Notes] 254

Absence of *Trichinella spiralis* in Rats in  
*J Parasitology* 1948, June, v 34, No 3,

Negative results were obtained with 418 specimens of 4 species

## SPRUE

SPIES, T D, GARCIA LOPEZ, G, MILANES, F, LOPEZ TOCA, R & CULVER, Belle  
Observations on the Hemopoietic Response of Persons with Tropical Sprue to Vitamin B<sub>12</sub> *Southern Med J* 1948, June, v 41, No 6, 523-5

In 1947 SHORR (*J Biol Chem*, 1947, v 169, 455) found in refined liver extracts a growth factor required for *Lactobacillus lactis* (LLD factor) which was present in an almost linear relationship to the unit potency of the extracts used in the treatment of pernicious anaemia. This is probably identical with a crystalline compound, vitamin-B<sub>12</sub>, and is believed to be partly responsible for LLD growth activity observed for liver extracts (RICKES *et al*, *Science*, 1948, Apr 16, 396). The positive response in pernicious anaemia as the result of small amounts administered to patients compared favourably with those obtained with folic acid and 5-methyl uracil (thymine), but neither of the latter has been found to prevent, or relieve, subacute combined degeneration of the spinal cord. It is with the effect of crystalline B<sub>12</sub> in patients with tropical sprue that the present communication is concerned.

The two patients with tropical sprue who were selected conformed to the criteria which have been laid down —

(1) There was macrocytic anaemia with a red blood cell count of 2.5 million, or less, and a colour index of over 1, (2) the bone marrow contained megakaryoblasts and had the typical erythroblastic arrest seen in macrocytic anaemia, (3) the diarrhoea was characterized by fatty stools, (4) glossitis and weight loss were present, and (5) the patients were otherwise untreated.

When the patients were placed on a diet devoid of meat, fish, poultry, milk and eggs, basic studies were completed and each was given a single dose of 0.008 mgm crystalline B<sub>12</sub> intramuscularly.

the technique used has certain limitations, it is important that experimental material of nematode origin should be the basis of methods of this kind.

The results are discussed in great technical detail and should be studied in the original but they were at variance with those of earlier investigators in most respects, especially in respect of lactones. More than 30 types of lactones were tested by the author but not one showed activity comparable with or even approaching that of santonin (itself a lactone). This contrast with the findings of other workers is attributed by the author to the use of different *in vitro* methods many of the observations reported in the literature have been prejudiced, in the author's opinion by the use of annelid material.

H J O'D Burke-Giffey

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H Har of Scott

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Onchocerciasis prevails in Mexico at heights of 400-1,200 metres above sea level and chiefly in the States of Chiapas and Oaxaca, which are sub-tropical with a heavy rainfall. The vector are *S. malinum ochraceum*, *S. calidum* and *S. meadus* the first which breeds in small collections of water moving slowly the two others prefer larger collections moving rapidly.

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  - (2) The bone marrow contained megakaryoblasts and had the typical erythroblastic arrest seen in pernicious anaemia.
  - (3) The disturbance was characterized by fatty stools.
  - (4) The patients and weight loss were present.
  - (5) The patients were otherwise unwell.
- When the patients were placed on a diet devoid of rice, poultry, fish and eggs these studies were completed and each was given a single dose of 0.008 mg crystalline B<sub>12</sub> intramuscularly.

In both patients (Cubans of 62 and 67 years) on the third day the soreness had disappeared from the mouth and tongue the appetite had returned the volume of the stools had decreased and they were less gaseous. On the sixth day the patient volunteered the information that they felt "wonderful."

The reticulocyte rise occurred on the fifth day and rose to a peak on the eighth.

P. MARRAS-BARR

## HAEMATOLOGY

WILLS, Lucy. Pernicious Anaemia, Nutritional Macrocytic Anaemia, and Tropical Sprue. A Discussion. *Blood* 1948 Jan. v 3 No. 1 34-56, [83 refs.]

Anaemia is only one aspect of pernicious anaemia nutritional macrocytic anaemia and tropical sprue the three diseases presenting fundamental differences which tend to be overlooked because of the similar response of the conditions to treatment with liver extracts or folic acid. Pernicious anaemia is a familial disease of persons of European descent the distribution of the disease corresponding to that of the racial groups affected, but occurring in all social classes of individuals. There are atrophic changes in the fundus and cardia of the stomach, with associated achylia gastrica an increased plasma bilirubin the presence of methaemalbumin in the plasma iron in the tissues and other evidence of a haemolytic factor and frequently subacute combined degeneration of the cord. The disease including the neural changes, can be successfully treated with crude or purified liver extracts given parenterally or orally with proteolysed liver extract by mouth with different preparations of horse's stomach by mouth and with digesta of beef muscle or autolysed yeast with normal human gastric juice. Folic acid and its conjugated forms produce haematological remission often suboptimal and an immediate sense of well-being but they are without benefit on the cord changes.

Nutritional macrocytic anaemia occurs mainly in tropical and subtropical areas, but the disease is associated with poverty with a low caloric largely or entirely vegetarian diet with pregnancy and lactation and with certain diseases, such as syphilis or particularly chronic malaria, which result in a hypertrophied reticulo-endothelial system. There are no significantly consistent changes in the gastric mucosa or secretion. There is no evidence of increased haemolysis except in areas with a high incidence of malaria. In the haemolytic type there are increased serum bilirubin values, a positive Schumm test an increased urobilin output, yellow coloration of the skin and fat splenomegaly and sometimes hepatomegaly and histological evidence of a hyperactive reticulo-endothelial system. Both the non-haemolytic and haemolytic types of the disease respond to crude liver extracts given orally or parenterally and to autolysed yeast extract. Relapses do not occur after cessation of treatment if the diet is maintained at a satisfactory level. Folic acid acts as in pernicious anaemia. The haemolytic type as in Macdonald's is sometimes resistant to treatment but some cases respond to enormous doses of liver extracts or Marmite.

Sprue has usually a gradual onset and is associated with residence in warm climate but affects Europeans other than pure Indians or Negroes. Many of the patients have been well fed and there is little evidence for direct nutritional origin for the altered intestinal absorption which conditions the ultimate deficiency. The disease is normally spread throughout but possible infective origin has been suggested by certain sporadic and locally concentrated outbreaks which have occurred. Lesions of the central nervous

system do not occur and apart from changes in the bone marrow and general inanition with decrease in organ weight, especially of the heart and liver, there are only slight anatomical changes detectable at autopsy. The disease responds to a high protein diet with liver extract or folic acid. Blood transfusion in the critically ill and sulphaguanidine where there is excessive diarrhoea may help.

In all three conditions, the classic picture of panhaemopoietic dystrophy is present, it is characterized by a megaloblastic erythropoiesis, a similar disturbance in the myeloid series with pathological macro-myeloid cells, and reduction and abnormality of thrombocytes. The general opinion is that the changes in the cells of the marrow and blood are identical in the three diseases. The panhaemopoietic dystrophy possibly results from a breakdown of an intracellular enzyme system, but the deficiencies causing the breakdown differ. In pernicious anaemia there is a genetic fault which results in a persistent and irreversible failure in the formation or absorption of the liver factor, and possibly of a neurotrophic factor. In endemic nutritional macrocytic anaemia there is an unconditioned food deficiency, the deficiency being in a factor other than the liver principle, possibly a co-enzyme present in or associated with good biological protein and the vitamin B<sub>12</sub> complex, in areas of high malarial incidence a haemolytic factor may also be present. Tropical sprue is associated with a functional disorder of the intestine, possibly a failure in phosphorylation of fatty acids, glycerol and glucose, but the cause of this functional breakdown is unknown.

F Murgatroyd

TROWELL, H C Tropical Macrocytic Anaemia and Nutritional Macrocytic Anaemia *South African J Med Sci* 1947, Jan, v 12, No 1, 21-31  
[57 refs]

There appears to be no valid distinction between macrocytic anaemia associated with pregnancy and nutritional macrocytic anaemia not associated with pregnancy. Similarly, there appears to be no real distinction between the macrocytic anaemia of pregnancy in warm climates and that of temperate regions. Some confusion arises because the blood and bone marrow have not always been clearly described in tropical anaemia and because many of the tropical cases are complicated by a light helminthic infection or mild relapsing malaria. In the present paper, the author analyses 63 cases of anaemia, of which 6 were associated with pregnancy, in Uganda. The aetiology of the anaemia in most of the cases was multiple, 80 per cent of the patients harbouring hookworms and 31 per cent showing malaria parasites. Most patients had a dual deficiency of iron and liver principle, giving rise to a dimorphic anaemia. Such an anaemia can often be determined from the appearance of a carefully spread thin blood film. With a dual deficiency, the film presents neither the picture of hypochromic cells with little anisocytosis such as is seen with pure iron deficiency, nor that of evenly stained flattened cells with much anisocytosis such as is characteristic of a pure deficiency of liver principle. In films of dimorphic anaemia, the central fields show solid-looking cells, perforated with one or more vacuoles, interspersed with a few densely stained thickened cells, and moderate increase of anisocytosis, while the peripheral fields show a few thickened cells and many flat cells, which are evenly stained, and there is increased anisocytosis. It might be expected that macrocytic orthochromic anaemia should, like pernicious anaemia, react to liver but not to iron, but out of 24 cases tested with crude liver extracts, 5 showed no response and 19 responded, whereas out of 14 cases tested with iron, 6 responded very well, 4 responded fairly well and 4 showed no response. In like manner, neither normocytic nor even microcytic anaemia appeared to be due always

to a single deficiency even microcytic anaemia responded to crude liver extracts. Although liver extracts were more effective than refined, neither was as effective as in pernicious anaemia, and it is, therefore, considered that the deficiency present in the tropical anaemia is not identical with that of pernicious anaemia. Further nutritional macrocytic anaemia as seen in Uganda can be distinguished from pernicious anaemia in the stained film: the bone marrow is not megaloblastic in the strict sense of the term, and indeed the anaemia is often not macrocytic—it may be normocytic or macrocytic and it is usually associated with some degree of iron deficiency and a varying parasitic infection.

F. Murgstroyd

WATSON Janet with the technical assistance of Albert W. STAHMAN & F. P. BILLO. The Significance of the Pandy of Sickle Cells in Newborn Negro Infants. *Amer J Med Sci* 1948 Apr., v 15 No. 4 419-23. [46 refs.]

The rarity of sickle cell disease in infancy is surprising in view of its frequency in later childhood, which suggests that the potentiality for sickling is incompletely developed at birth. Of 228 negro mothers 18 (8 per cent) showed sicklaemia, and in those affected the percentage of red cells sickling was usually 100 and exceeded 84 in every case. Of their 228 newborn infants, 19 (8.4 per cent) showed sicklaemia, and in the affected infants the maximum sickling varied from 0.5 to 29.5 per cent. of the red cells with a mean of 11 per cent. Sickling of the infants' red cells often required 48 hours to reach a maximum instead of the 4 hours which usually sufficed for the mothers' red cells. Presumably a lower oxygen tension is required to sickle infants' cells and as there is a significant shift to the left of the oxygen dissociation curve of oxyhaemoglobin at birth which only gradually reaches adult values at the age of six weeks, the longer period necessary for sickling in the newborn may be due to a greater affinity of foetal haemoglobin for oxygen compared with the adult type of haemoglobin. This would not however account for the low percentage of sickled red cells in newborn infants since the maximum percentage of sickling could not be raised by use of a gas chamber method in which oxygen was excluded entirely from the system. Simple immaturity of the cells is not a sufficient explanation either because although normoblasts and reticulocytes sickle less readily than mature erythrocytes the blood of the infants contained no high percentage of immature cells. There is however evidence that human foetal haemoglobin differs chemically from adult haemoglobin probably in the chemical structure of the globin. It is suggested that foetal haemoglobin is unable to produce sickling and that the sickling trait and the percentage of red cells showing the sickling trait progressively increase as red cells containing the adult type of haemoglobin are produced. The foetal haemoglobin disappears at the age of about 4½ months and the life span of the erythrocytes is about 4 months, so that if adult haemoglobin began to develop at birth four months would lapse before it would entirely replace the foetal haemoglobin. One infant observed over such a period developed 60 per cent. sickling at 4½ months compared with only 6 per cent. sickling at birth. Normally an oxygen tension of 45 mm. Hg is the threshold for sickling, and undoubtedly the lower oxygen tension that occurs after birth should cause complete sickling and thus be incompatible with life. Therefore at birth erythrocytes of the pathological findings of sickle cell anaemia in the topsies of newborn or stillborn infants. It is moreover that the foetal haemoglobin lacking the sickling property of adult haemoglobin prevents the uterine environment of sickle cell disease from developing after and partially protects the infant during the first four months of life during which time the foetal haemoglobin gradually disappears from the blood.

F. Murgstroyd

VALENTINE, W N & NEEL, J V A Statistical Study of the Hematologic Variables in Subjects with Thalassaemia Minor *Amer J Med Sci* 1948, v 215, No 4, 456-60, 3 figs [13 refs]

Cooley's anaemia, an inherited haematological disorder of people of Mediterranean stock, may be severe, progressive and almost invariably fatal, or relatively mild, it is suggested that the terms thalassaemia major and thalassaemia minor be applied respectively to the two types. The major variety occurs in about 1 in 2,400, while the minor variety occurs in 1 in 25 births to persons of Southern Italian or Sicilian stock in Rochester, New York. The minor variety occurs in well-nourished persons with hypochromic microcytic erythrocytes, which are frequently oval or appear as target cells, basophilic stippling is common. Haemoglobin and haemocrit values are usually but not invariably low, and by comparison the total number of erythrocytes is disproportionately high. The erythrocytes show increased resistance to haemolysis by hypotonic saline. There may or may not be leucocytosis, reticulocytosis and elevated icterus index, or splenomegaly. In 82 persons with thalassaemia minor, there was an average deficiency of 2 to 3 gm of haemoglobin per 100 cc of blood, the defect being superimposed on the normal levels of haemoglobin for male and female so that the males showed higher haemoglobin values than did the females similarly affected. The tendency for persons with thalassaemia minor to have relatively elevated erythrocyte counts was confirmed, only 2 out of 58 of the adult patients having erythrocyte counts below 5 million per cmm, in 48.3 per cent of thalassaemic females and in 85.8 per cent of thalassaemic males the counts were above 5½ million per cmm, while 57 per cent of the males had counts above 6 million per cmm. The mean corpuscle volumes and mean corpuscular haemoglobin values were markedly below normal. The mean corpuscular haemoglobin concentrations were not so markedly lowered, showing that although the red cells are small in volume, each cell for its volume is only moderately deficient in haemoglobin.

F Murgatroyd

STOWE M Report on Anaemia amongst the Women of Bhopal *J Ass Med Women in India* 1948, Feb-May, v 36 No 1 5-20 5 graphs

## VENOMS AND ANTIVENENES

CECCALDI, J & TRINQUIER, E Recherches sur la toxicité des glandes salivaires de divers Colubridés aglyphes et opisthoglyphes africains [Study of the Toxicity of the Salivary Glands of different African Aglyph and Opisthophlyph Colubrids] *C R Soc Biol* 1948, Apr, v 142 Nos 7/8, 440-41

The authors studied the toxicity of the salivary glands of 8 species of Aglypha and 8 of Opisthophlypha by injecting saline suspensions of the macerated glands into mice in successive dilutions. All the Aglypha except one killed less than 4 mice and that one killed 8. 5 of the 8 Opisthophlypha killed respectively 16, 32, 80, 320 and 5,120 mice. Two species of Opisthophlypha killed less than 4 mice and one killed 8.

The Aglypha studied are not likely to be harmful to man. On the other hand, certain of the Opisthophlypha investigated seem capable of causing fatal accidents in man. This applies especially to *Dipsadomorphus blandini*, which killed 320 mice in the tests and *Elapops modestus* which killed 5,120.

H J O'D Burke-Gaffney

TRIQUIER, E. & CECCALDI, J. Toxicité des glandes salivaires chez quelques Viperidés africains à leur naissance. [Toxicity of the Salivary Glands of some African Vipers at Birth.] *C. R. Soc. Biol.* 1948, Apr., v 14, Nos. 7/8 441

It is known that new-born venomous snakes have well-developed salivary glands and venom comparable with that of adults but few investigations are recorded on quantitative studies, particularly in African snakes.

The authors investigated this point in the new-born of two species *Buis gabonica* and *Buis masicornis*. Successive dilutions of saline emulsions of the glands were injected into mice.

In the case of *B. gabonica* emulsions from 2 glands were enough to kill 640 mice but not 1,280 the venoms were lethal for at least 11 kgm. of animal. Similar emulsions from new born *B. masicornis* killed only 4 mice its venom was thus far less toxic than that of *B. gabonica*.

These differences were maintained in adult life experiments showed that venom from a large adult specimen of *B. gabonica* was lethal to mice at the order of 485 kgm. of animal, while in the case of *B. masicornis* the figure was 110 kgm.

H. J. O. D. Burke-Gaffney

CONSTANT, Y. & GOUTIER, P. Sur les phénomènes d'araignisme provoqués par *Latrolectus menardi*. [Symptoms of Bites by *Latrolectus menardi*.] *Bull. Soc. Path. Exot.* 1948, v 41, Nos. 3 & 234-7

The specific name *menardi* was given to this spider because it is a *Marid*, a word indicating red spots behind. Bites by it are generally dreaded by both indigenes and by Europeans. Detailed accounts of three cases are given: one patient was bitten on the inside of the left thigh, one on the right instep, and one on the back. The symptoms in the first and third were similar: pain at first local but soon extending widely over the body but greatest in the legs, no loss of reflexes, profuse sweating, retention of urine, albumin present in the small amount which may be passed and a little blood, an urticarial pruriginous rash on the 3rd or 4th day, slight rise of temperature at first, later falling below normal, and recovery in 5-8 days. In the second patient the early symptoms were the same, but signs of cardiac failure set in and in spite of all the remedies tried death occurred 27 hours after the infliction of the bite. No work has yet been done on the venom of this spider and treatment at present is purely symptomatic, to ease the pain, check the sweats and combat the failing heart.

H. Harold Scott

## DERMATOLOGY AND FUNGUS DISEASES

CAHOE, F. W. The Effect of Hydrogen-Ion Concentration on the Yeastlike Phase of *Histoplasma capsulatum* (Darling). *Pub. Health Rep. Wash.* 1948, June 4 v (3) No. 23 33-40, 26 [10 refs.]

The purpose of the author's experiments was to find liquid medium suitable for the propagation of *Histoplasma capsulatum* in its paramecium, yeast-like form. Five strains of the fungus were tested for growth on three different media over a wide range of pH at incubation temperatures of 25°C. and 37°C. (The fungus cannot vegetate in the yeast form at 25°C. on any medium.)

The following results refer to cultures inoculated at 37°C. On a glucose (1 per cent.) broth medium the yeast form showed a marked tendency to revert



to the mycelial form under all conditions of the test, so this medium was discarded as unsuitable. On beef-extract-broth the best results were obtained at the hydrogen-ion concentration of pH 7.3, but in the higher and lower pH ranges there was a slight but increasing tendency to develop rudimentary mycelium. "Difco" brain-heart-infusion-broth proved the most satisfactory medium, with optimal conditions in the pH range 7.4 to 7.5, but again in the higher and lower pH ranges there was a tendency towards reversion to the mycelial form, this was greater in the lower pH range, but in the higher range it was accompanied by retardation of the growth of the yeast form.

J T Duncan

RAWSON, A J, COLLINS, L H, Jr & GRANT, J L. **Histoplasmosis and Torulosis as Causes of Adrenal Insufficiency** *Amer J Med Sci* 1948, Apr., v 215, No 4, 363-71, 5 figs [25 refs]

A tabular analysis is given of eight previously published cases of histoplasmosis (*Histoplasma capsulatum*) in which necrosis of the adrenal glands induced symptoms of adrenal insufficiency, and eleven other cases of histoplasmosis and one of torulosis (*Cryptococcus [Torulosis] neoformans*) in which the adrenal glands were involved without symptoms of adrenal insufficiency, are noted. This is followed by detailed reports of the ninth case of adrenal insufficiency due to massive necrosis of the adrenals by *H. capsulatum*, and a case, claimed as the first, of torulosis characterized by adrenal insufficiency. The latter was only diagnosed as torulosis at post mortem examination. In both patients, who were women aged 62 and 41 years, respectively, excessive weakness was the first symptom.

Attention is drawn to the fact that in the cases of adrenal failure due to *H. capsulatum*, the ratio of 2 males to 1 female is the same as that noted in Adamson's disease from all causes although the age group (39 to 63) is somewhat higher than that for Adamson's disease (30 to 50).

G C Ainsworth

SMITH, C E, WHITING, E G, BAKER, E E, ROSENBERGER, H G, BEARD, R R & SAITO, Margaret T. **The Use of Coccidioidin** *Amer Rev Tuberculosis* 1948, Apr, v 57, No 4, 330-60, 2 figs [56 refs]

This detailed study of coccidioidin and its diagnostic use should be read in the original. After dealing with the relatively crude preparations of coccidioidin used in the earlier work on coccidioidomycosis, the authors recommend the method of preparation in common use in the United States at the present day. This consists in growing selected strains of *Coccidioides immitis* for 2 months at 22°C in a modification of the synthetic, liquid, asparagine medium devised for the production of tuberculin. The culture liquid is then filtered through a Seitz filter and the sterile filtrate, preserved with 1:10,000 merthiolate, constitutes the stock coccidioidin. As the asparagine medium does not cause dermal reactions, test control injections are not necessary.

The active principle of coccidioidin, which is mainly or entirely of polysaccharide nature although a small amount of apparently non-protein nitrogen is always present, is extremely stable and will withstand a temperature of 120°C in the autoclave for 10 minutes, or flowing steam for an hour. If sterile and undiluted it can be kept in cold storage for an indefinite time without loss of potency and in fact, a sample left at air temperature in a warm climate for nearly 9 years was found to be fully potent for the skin test. Even when diluted to 1:100, it can safely be kept in cold storage, but bacterial contamination may render it inert or may even cause it to give spurious positive reactions.

Coccidioidin should be standardized by intradermal tests on known human reactors, non reactors and equivocal reactors. The test dosage recommended is 0.1 ml. intradermally of a 1:1,000 dilution for active early cases, or down to 1:10,000 if erythema nodosum, indicating high sensitivity is present in the disseminated disease in which sensitivity may be very low or absent. A 1:10 dilution may be necessary and for epidemiological survey work a 1:100 dilution may be used on the average. The reaction is sufficiently specific for its purpose and it is of the delayed type like the tuberculin reaction. It is nearly always discernible at 4 hours, reaching its maximum at about 76 hours but it may develop earlier or later and, therefore interval readings should be taken. Dermal sensitivity to coccidioidin cannot be induced passively by injecting the serum of a reactor into the skin of a non-reactor nor does the skin become sensitized by the repeated injection of even strong doses of coccidioidin into the skin of a non-sensitive subject although he may become sensitive later from a natural infection. Dermal sensitivity usually appears a few weeks after infection, but its onset may be delayed. It may be of only transient duration, but it usually lasts for many years. J. T. DUNN

NABARRO J. D. N. Primary Pulmonary Coccidioidomycosis. Case of Laboratory Infection in England. *Lancet*. 1948, June 20, 962-4 2 figs. (28 figs.)

See *Bulletin of Hygiene* 1948, v. 22, 688.

RUSO E. & GOMES R. P. Novas observações de esporotricose. [Fresh Observations on Sporotrichosis.] *Hospital Rio de Janeiro*. 1948 Feb. v. 33 No. 2, 15-22, 9 figs.

Four cases are briefly recorded: one a girl of 8 years, with a warty lesion of the right cheek; one, a girl of 17 years, with a lesion of the left hand between the thumb and forefinger; third, a boy of 12, with lesions of the left hand and forearm; the fourth, an adult woman with a small lesion on the ulnar side of the base of the right little finger and later two others near the cubital fossa.

The chief interest of the paper, however, is that all were diagnosed by isolation of *Sporotrichum schenckii* grown on Sabouraud dextrose medium, a blackish pigment. On transfer to ordinary agar pH 6.6 it grew well but white, with no pigment at all and continued to do so on this medium. When, however, it was retransferred to Sabouraud's medium again it again assumed the coloured growth. H. HAROLD SCOTT

## HEAT STROKE AND ALLIED CONDITIONS

STEWART W. Effects of Heat with special reference to its Occurrence in British Troops in the Persian Gulf Area in 1941-42. *J. Roy. Army Med Corps* 1943, May v. 90 No. 5 175-83 3 figs. 16 figs.

In the summer of 1947 there were 168 cases of heat stroke with 32 deaths and 1,935 cases of heat exhaustion with 13 deaths. Among the British troops in the Persian Gulf area 14.9 per cent of the total British strength was affected. The author gives a brief description of these cases and considers them in relation to recent work on the physiology of man in the heat and on the pathological changes found in men suffering from the effects of heat.

The author distinguishes four types of heat effects: (1) Heat exhaustion; (2) Subacute effects of heat; (3) Heat cramps; and (4) Acute heat stroke. The

line of distinction between the first three is difficult to draw, but subacute effects, if untreated, may develop into heat stroke, which is acute hyperpyrexia

Immediate treatment is essential with controlled replacement of water and salt, and, for hyperpyrexia, active cooling. The importance of suitable clothing, adequate rest, proper acclimatization and a sufficient intake of salt and water in avoiding heat casualties is emphasized. Periodic medical examinations of all those serving in hot areas is advised.

[This paper would serve as a useful introductory review of the subject, but it adds nothing to our knowledge of heat effects. The author's classification of the different types of effects of heat is not universally accepted, 'it is the same as that given in the official memorandum reviewed in this *Bulletin*, 1944, v 41, 74.]

W S S Ladell

### MISCELLANEOUS DISEASES

COUTINHO, A. Eosinofilia tropical [*Tropical Eosinophillia*] *Hospital Rio de Janeiro* 1948, Jan, v 33, No 1, 77-85 [25 refs]

The author records five cases which presented the symptoms of tropical eosinophilia—asthmatic attacks, eosinophilia ranging from 56 to 71 per cent in a leucocytosis from 12,000 to 26,500 per cmm. Unfortunately these records make confusion worse confounded rather than elucidate this vexed question. Each of the cases is given in detail, one disappeared and could not be followed up, the others cleared up under different forms of treatment. Two were suffering from amoebiasis and were treated with emetine, enterovioform and carbarsone, another, a medical man, seemed to be an ordinary case of bronchial asthma which cleared up with ascorbic acid and calcium. The only positive finding here was a strong reaction to tuberculin, 1:10,000. The remaining patient improved on penicillin and sulphadiazine, but still suffered with slight attacks of nocturnal asthma and was given an autogenous vaccine of *N. catarrhalis*, *Pneumococcus* and *H. influenzae* and improved markedly when abdominal pain elicited the fact that he had a duodenal ulcer. On the idea of a possible Löffler's syndrome he was given arsenicals and the dyspnoeic attacks disappeared completely though he still had some stertor. [An interesting series of cases, but leaving the subject as obscure as before.]

H Harold Scott

FERRO-LUZZI G. Studio sui fenomeni di malnutrizione in Eritrea. Nota II [*Malnutrition in Eritrea*] *Boll. Soc. Ital. di Med. e Igiene Trop.* (Sez. Eritrea) 1947, v 7, Nos 5/6, 483-94, 1 fig. English summary.

This article is an informative and interesting account of a disease known for many years (the author says "for centuries") among those consuming the seeds or flour made from the seeds of a plant known as "seberè". It grows on the upper levels and is abundantly cultivated and used fresh or cooked, alone or with other kinds of flour for making cakes (*chiuccià*) which are eaten by all and sundry. It is cheap, easily cultivated, needs little water and is not liable to damage by acarides. Usually only a small proportion is used, mixed with other flour, but at times when other flour is scarce the proportion is higher. This happened after an invasion by locusts in 1946. If more than 50 per cent of the flour is used for making these cakes symptoms appear in 20-100 days according to the quantity eaten.

Seberè was identified as *Lathyrus sativus*, some samples are adulterated with *Vicia sativa*, but samples sent to the Agricultural Department of Eritrea were

not so adulterated. The symptoms were those of spastic paraparesis characteristic of lathyrism and affected males and females of all ages, but more particularly the poorer classes who consumed this flour in larger quantities. Details are given of six patients and an illustration of one of them showing the attitude and gait of typical spastic paraparesis. Five were males aged 7, 8, 17, 25 and 33 years, and one woman aged 30. There was no disturbance of vision, no psychic symptoms, no change in the cerebro-spinal fluid. Very rare was any affection of the upper limbs or of the plantar reflexes. Vitaminosis did not seem to play any part primarily, but it may aggravate the basic lathyrism; the administration of vitamin had no curative effect. Prophylactic measures are obvious but attempts at cure have altogether failed.

H. H. H. H. H. H.

BLOSS, J. F. E. Symmetrical Gangrene in an African. *Correspondence J. Brit. M. J.* 1948, July 3, 52.

A fatal case in Sudanese aged 35 (see this *B. Ill.* 1947 44 937).

BURKITT, D. I. Spontaneous Rupture of the Spleen. *East Afr. M. J.* 1948, Apr. v, 3, 4 167-4 (22 figs.)

A review of the causes.

## PROTOZOOLOGY GENERAL

BUTLER, J. On the Recovery of Protozoa and Eggs of some Species of Helminths in Human Faeces. *J. Parasitology* 1948, Apr. 31, 38, 101-7 (10 refs.)  
[See this *Bulletin* 1947 v 44 1101]

SEAMAN, G. R. Penicillin as an Agent for Sterilization of Protozoan Cultures. *Science* 1947 Oct. 3 377

The author concentrated *Colpoda macropoda* by centrifugation and washed the organisms three times with sterile Hahnert's solution (Phys. Zool. 1932, 5:491). A few drops of the washed concentrate were added to 3 per cent. sterile Disco proteose peptone solution containing 5,000 units of penicillin G. After 12 hours in the penicillin solution, the organisms were transferred through three successive washes of 3 per cent. proteose peptone. A drop containing the organisms and the fluid from the last wash was plated on agar in 8 tests; no bacterial growth was seen and the colpoda were apparently uninjured by 12 hours' exposure to this concentration of penicillin.

It seems that this method may be used to obtain sterile cultures of most protozoa but the survival time of each species, the minimum concentration of penicillin must be ascertained separately. At times very short lower concentrations are required. Preliminary tests suggest that *Paramecium caudatum* remain vigorous for 5 hours in a solution of 500 units of penicillin G, but is killed in 12 hours at the concentration used. It is added that the process does not require constant sterile technique, the number of animals recovered and the number of transfers is reduced to a minimum.

H. J. O. D. H. H. H. H. H.

TEDESCHI, G. G. An anti-toxic action of a pigment from *Paramecium* against *Ascaris*. *J. Parasitol.* 1948 Mar. 34 No. 1 59. English summary (4 lines)

In the author's laboratory a strain of *Paramecium* was isolated from culture contaminated by it. It was found to produce a pigment having cytotoxic

definite action on certain protozoa. On further study a method of extraction of this pigment was devised. The mould was cultivated on a liquid Sabouraud's medium in a Roux flask at 30°C till it had developed fully. The growth was then removed very carefully to avoid damaging it and detaching the spores, and was then placed to dry at a temperature of 40°C. When completely dried it was extracted with chloroform in a Soxhlet apparatus till the extracting solvent came away colourless. When concentrated the solution had a deep yellowish-brown colour, it was allowed to cool and treated repeatedly with phosphate solution at pH 7.5 when it became yellow. The chloroform was then driven off and the product brought to pH 3 with HCl or H<sub>2</sub>SO<sub>4</sub>, a flocculent precipitate formed and on centrifuging a greenish-yellow product was obtained which was repeatedly washed with distilled water, brought up to pH 6, then dried, and NaOH cautiously added to obtain a clear liquid of an intense brown colour at pH 2.5.

Testing this, the author found that it had no action on *Bact. coli*, very little on *Staph. pyogenes aureus*. It was haemolytic but not if serum were present, in fact, haemolysis could be prevented by addition of serum. On protozoa the following results were observed. *Polytoma uvella* (a flagellate) was fixed at once, *Paramecium* was immobilized but not permanently, *Hartmannella hyalina*, a coprozoic amoeba, was immobilized with extended pseudopodia, *Giardia enterica* [*G. intestinalis*] moving in liquid faeces was immobilized and killed. *Trypanosoma lewisi* and *T. gambiense* in blood were rapidly immobilized. It was active on these also when injected into experimental animals, white rats and guinea-pigs, in a dose of 3 cc of the solution per 100 gm body weight, and apparently caused no systemic disturbance. *H. Harold Scott*

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## ENTOMOLOGY AND INSECTICIDES GENERAL

LAIRD M. A Method of securing Living Mosquitoes to Mounts in Studies of Problems concerning Flight. *Science* 1948 June 18 656 1 fig

ABRAHAM O. K. *Anopheles* (*Anopheles*) *kyondawensis* n.sp. from Lower Burma. *Med. J. Malaya* 1947 Mar v 1 No 3 173-6 5 figs

NERI, I. Osservazioni morfologiche sul pretarso delle culicine [A Morphological Observation on the Pretarsus of a *Culex*]. *Riv. di Parassit.* Rome 1948, June, v 9 No 2, 93-6, 2 figs

The English summary appended to the paper is as follows —

'The author reports the description of a peculiar organ present in the pretarsus of *Culex pipiens autogenicus*'

MACFIE, J. W. S. Some Species of *Culicoides* (Diptera, Ceratopogonidae) from the State of Chiapas, Mexico. *Ann. Trop. Med. & Parasit.* 1948, Apr, v 42, No 1, 67-87, 10 figs

The author has examined a portion of a large collection of Ceratopogonidae estimated to contain 20,000 specimens. Most of the material was collected by Dr A. Dampf from May to July, 1935, in Mexico.

The portion examined includes 3,335 specimens of *Culicoides* of which 97 per cent were *C. guttatus*. (It was in specimens of this species that Dr Dampf found developing filariae in 1936.) The remaining 3 per cent contained sixteen other species, ten of them are new and are described in this paper. A key is

given for the identification of some sixty species of *Culiscoides* (females) likely to be found in the Caribbean area, including also species occurring in regions ranging from southern Mexico to Brazil.

H. S. LECHE

**TAEODOR O.** Classification of the Old World Species of the Subfamily Phlebotominae (Diptera, Psychodidae). *Bull. Entom. Res.* 1948 May v 39 Pt. 1 83-115 15 figs. & 2 pls. [33 refs.]

The present paper is a valuable review of the systematics of the sand flies (*Phlebotomus*) of the Old World, written by an authority on the subject. These insects have not been monographed since the paper by LAROUSSE [this *Bulletin* 1921 v 18 198]. At that time 37 species and 8 varieties were known; the present author deals with 127 species and 34 varieties of which he has seen the greater part himself.

It might be said that some previous workers on the subject have tended to be "Phlebotomist" rather than Dipterists, for they have developed a terminology in connexion with sand flies alone with little regard for terms which are used for the Diptera generally. The present author takes account of comparative anatomy which will entail a few alterations in the use of technical terms. With regard to buccal cavity and pharynx he is conservative basing his view on the work of SYMONDS (*Principles of Insect Morphology* 1935, McGraw Hill New York) he does not accept "pharynx" and oesophageal pump terms put forward by JONING [this *Bulletin* 1928 v 5 825] for certain structures in *Culiscoides* which are plainly identical with those in *Phlebotomus*.

The earliest clear reference to these insects is that made by Scopoli in 1763. The growth of knowledge since that time and the earlier system of classification are here reviewed and on a basis of this earlier work much of which is still valuable the author puts forward his own views. He classes *Phlebotomus* and the other blood sucking genera immediately related to it as a sub-family the Phlebotominae of the family Psychodidae. In doing this he rejects a proposal made by ADLER and himself [this *Bulletin* 1930 v 77 189] to create a separate family for the blood-sucking forms and we are glad to see that he has done so. The other three sub-families of the Psychodidae contain no biting forms (the record of biting by *Pericoma lasioides* Taylor 1915 being rejected).

The Phlebotominae are divided into four genera *Phlebotom*, *Sergentomyia*, *Lutzomyia* and *Brumptomyia*. Of these the last two are exclusively American the first two with which this paper is concerned are characterized on the following points among others—

*Phlebotom* s. Rooulard, 1843.—Species without armature in buccal cavity. Pharyngeal armature generally similar in male and female. Hair on dorsum of abdomen mostly in erect tufts. Spermatheca completely or incompletely segmented. This genus contains nearly all the species which feed on mammals and all those which are implicated in the transmission of human infections.

*Sergentomyia* Franca and Parrot 1920.—Species with a buccal armature marked sexual dimorphism in buccal and pharyngeal armature. Spermatheca generally smooth or crinkled tube or capsule, not completely segmented in a few forms. Only a few members of this genus are known to bite man (*S. aethiops africana* and *S. h. h.*). It is known that some feed on bird and reptiles.

The author defines a number of sub-genera some of which are new both in *Phlebotomus* and *Sergentomyia* naming the type species of each and providing a key to the sub-genera. The paper concludes with a list of all the Old World

species and authorities with a few words on the geographical distribution of each. A number of names are sunk as synonyms for reasons not given here. The paper is concluded with a list of works "concerned with classification" and with two excellent plates of photomicrographs showing characteristic details of structure. P A Buxton

THEILER Gertrud Zoological Survey of the Union of South Africa Tick Survey—  
Part I Onderstepoort J Vet Sci & Animal Industry 1948, Mar, v 23,  
Nos 1/2, 217-31 4 folding coloured maps

ACOSTA BAYARDO, R Informe preliminar acerca de infestación por miguas o  
*Tunga penetrans* en el Estado de Nayarit [A Preliminary Note on Infes-  
tation by *Tunga penetrans* in the State of Nayarit] Medicina Mexico  
1948, June 25, v 28 No 558, 251-3

DRAN, G M Armillifer Armillatus A Note on Three Cases of Calcification  
of the Cysts in Man Brit J Radiol 1948, July, v 21, No 247, 342-5,  
6 figs [17 refs]

The diagnosis of porocephalosis in the living subject is rare, but cases have been reported from time to time, most of these have been concerned with calcified nymphs of *Armillifer armillatus*, which probably do not produce symptoms as a rule, but cases in which pathological effects were noted have been recorded [this Bulletin, 1947, v 44, 136, 626].

The present author, from the Royal Liverpool United Hospital, discusses this form of infestation and refers briefly to the literature. He then records three cases in which multiple calcified nymphs were demonstrated radiographically in natives of West Africa.

The first patient was complaining of pain in the back and osteoarthritic changes were found in the spine. Very many calcified nymphs of *A. armillatus* were demonstrated in the abdominal cavity and there were one or two in the upper zone of the right lung. It is not considered that the symptoms were due to the presence of the nymphs. The second patient had suffered from a cough and pain in the chest for a month. radiography showed numerous calcified nymphs over both lung fields. The third case had similar symptoms and radiological appearances.

All these findings are illustrated with X-ray photographs in the text. When the nymphs are seen *en face* they are unlike any other calcification, but when seen "end on" over a muscle area, they might easily be confused with the cysts of cysticercosis. Atypical forms might be confused with calcified glands, calculi and the like, but calcified tuberculous foci are not common in natives of West Africa.

The author refers to the paucity of information regarding such calcified nymphs in the standard text books and he stresses the need for keeping the condition and its features in mind. Once it has been seen, it will not readily be forgotten and after the first of his cases had been recognized there was no difficulty in identifying the others.

The living larvae may be another cause for transient pneumonias and haemoptyses. The author suggests that a skin test might be developed to detect the living parasite. It is likely that with an extension of radiographic services in the tropics, more cases will come to light.

The author's present three cases bring the total record of radiographically demonstrated cases up to five.  
H J O'D Burke-Gaffney

PATTON R. L. & SARKARIA D. S. Preparation of Standard Films of DDT Crystals for Toxicity Studies, *Science* 1948, June 13 63: 1127.

See also p. 884 HARTIG & FAIRCHILD The Control of *Phlebotomus* in Peru with DDT

ILADJINIKOLAU J. & BUSVINE, J. R. Toxicity of Limewash containing DDT or "Gammexane" to Mosquitoes (*Aedes aegypti* L.) *Bull. Entom. Res.* 1948 May v 39 Pt. 1 179-83 1 fig.

In many rural malarious districts, the dwellings have mud or plaster walls, brightened by an annual coat of whitewash. The object of the tests described was to investigate the feasibility of incorporating DDT or *gamma* BHC in limewash to give a residual action against mosquito adults.

The tests were done in one-foot-cube cages, each with a screen and window in the front to introduce and watch the insects. The walls, which were removable, were made of pieces of Essex board one foot square (this is an absorbent material offering difficulties to applying residual films of insecticides). The Essex boards could be treated in various ways and applied to the cage framework for test. Mosquitoes were introduced for various periods of exposure and then removed to a clean cage; the mortality was determined after 24 or 48 hours. During the exposure mosquitoes were free to fly or to settle on the untreated portions of the cage, which comprised about thirty per cent. of the total internal surface. *Aedes aegypti* were used as the test insects on account of the ease in producing large numbers in the laboratory throughout the year.

The experiments were made with applications to the walls of (a) DDT wettable powder mixed with lime to give a white wall coating, and (b) this treatment was compared with DDT applied in kerosene solution at the same rate (100 mgm./sq. ft.). In the whitewash application an eventual mortality of 85-90 per cent. was obtained after an exposure of two hours; the result with the kerosene solution application were inferior. Equally high kills were obtained with much lower rates of *gamma* BHC (8 mgm./sq. ft.) applied in a stable powder mixed with limewash.

Repeated tests made at intervals indicated that both the DDT and *gamma* BHC whitewash applications remained highly effective up to about 6-8 weeks under temperate conditions. A higher rate of *gamma* BHC (40 mgm./sq. ft.) gave a complete kill with a one-hour exposure after twenty-two weeks interval. The DDT treatment was not tested after eight weeks until seven months, at which point it showed signs of deterioration. J. R. B.



Experience is necessary to overcome the interruption of vision due to respiratory movements, and to interpret the observations on circulatory changes. The author suggests that the flow through the splenic pulp of mice is by tortuous channels, constant in position, and ramifying between the splenic cells. There is no evidence for a closed circulation.

All observations may represent the normal modified by anaesthesia, exposure, disturbance of surface pressure, temperature etc. The illumination used is insufficient for the photography of moving tissues. *E T Renbourn*

## REPORTS, SURVEYS AND MISCELLANEOUS PAPERS

WORTH, H I. *The Age Question among Asiatic Girls in Malayan Courts of Law*  
*Med J Malaya* 1947, June, v 1, No 4, 252-71

European standards on height, weight, centres of ossification and date of onset of puberty are not applicable to Asiatic girls in Malaya. "Asiatics" could not be grouped together, racial groups showed differences, especially the three main groups—Chinese, Indians and Malays.

Nine tables are furnished showing the average and maximum and minimum heights and weights of the four main groups examined, as well as of some of the minor groups, arranged according to ages from 5 years to 19 years. The conclusion is drawn that the European standard of height and weight is higher than that of any of the Asiatic races in Malaya, a greater difference is noted in the weight than in the height and there is a much greater range in the weight of Asiatics but a smaller range in the height.

Onset of menstruation tended to be earlier in the local Asiatic groups than in Europeans.

The date of eruption of permanent teeth appeared to be earlier among Asiatic races. No deciduous teeth were found at the age of 12-13 years, the lower second molar was seen in all those examined at that age and the whole lower set was present, excluding the third molar. Earlier eruption of the canine teeth was also noticeable.

Details should be consulted in the original by all those interested in medico-legal work in tropical countries. *P A Clearkin*

MÉGROZ R L. *Ronald Ross as Medical Discoverer and Poet*. *J National Malaria Soc* 1948, June, v 7, No 2 85-94 2 figs & 1 pl.

## BOOK REVIEW

SERGEANT, Edmond & SERGEANT, Etienne. *Histoire d'un marais algérien*  
[The History of an Algerian Marsh] 293 pp, 18 pls, 3 folding maps & numerous text figs. 1947. Alger. Institut Pasteur d'Algérie.

In 1911 the authors with Dr E Roux were motoring along the Mitidja Plain. They passed a derelict farm that had had a tragic history—a promising enterprise that had been brought to disaster by malaria. That experience prompted Dr Roux's suggestion that the Pasteur Institute of Algiers should seek out some similar place, not too far from the Institute, that malaria had made uninhabitable. It should be reclaimed, freed from its malaria and brought back into cultivation, as a practical demonstration of what recently acquired

knowledge of the epidemiology of malaria might accomplish. Dr Roux promised to provide the funds necessary for the acquisition of such a property. The 1914-18 war intervened and it was only in 1927 that the Pasteur Institute obtained possession of land in every way suitable for the purpose of the experiment. 700 hectares of marshland in the Mitidja Plain, 25 km. south west of Algiers the *Marais des Ouled Mendil*. Malaria had made it uninhabitable. *peroplasmosis* had prohibited its use as a grazing ground.

The *Histoire des Marais Algériens* a charming volume describes that marshy waste as it was, and gives a graphic account of the measures that step by step succeeded in transforming it into a malaria free flourishing agricultural property. Today it is a very valuable adjunct to the Pasteur Institute of Algiers. Colmatage, drainage, road making, tree planting, farm building, agriculture well sinking were all systematically taken in hand. Forty six Europeans have dwelt in that once malaria infested spot, the average length of stay being four years. All remained free from malaria infection. European cattle vaccinated against *peroplasmosis*, thrive.

This great achievement is very worthily commemorated in this lyrical volume enriched with delightful illustrations and innumerable apt quotations. The history is much more than a record of achievement. It provides interesting information about Algerian history, ancient and modern, archaeology, geology, fauna, flora, man's tribute to malaria, the history of malaria research and antimalarial methods. Its perusal is a pleasure to which the wealth of apt quotations from the classics contributes much.

Vernon Hyde

We record with the greatest regret the death of  
Lt Colonel W. F. HARVEY and Dr C. M. WENYON.

Lt Colonel Harvey who died in Edinburgh on September 11 1948 contributed abstracts of bacteriological paper to the *Tropical Disease Bulletin* from 1925 onward and was later sectional editor for cholera and plague prior to the time of his death.

Dr Wenyon died in London on October 4 1948. He was editor of the *Health Law Bulletin* in 1911 and subsequently for the last 14 years was sectional editor of the *Tropical Diseases Bulletin* for his humanism and for his work.

## BUREAU OF HYGIENE AND TROPICAL DISEASES

TROPICAL DISEASES  
BULLETIN

[No 11]

1948

Vol 45]

## SUMMARY OF RECENT ABSTRACTS\*

## IX LEPROSY

*Epidemiology Transmission*

In the *British Medical Journal* (p 719) is an account of 6 cases of leprosy which occurred in Britain in persons returned from the Far East. The importance of bearing leprosy in mind in cases of resistant skin lesions is emphasized.

In a survey of 42,811 school children in British Guiana WHARTON (p 720) found 94 cases of leprosy, 91 of which were early nerve cases. FLOCH and DE LAJUDIE (p 322) estimate that the incidence of leprosy in French Guiana is about 65 per 1,000, with the highest rates at the age of 6-10 years. Family infections and school infections are common. The same authors (p 589) give a detailed account of the progress of a considerable number of leprosy patients in French Guiana. They record incubation periods as short as 9 and 15 months in two infants. The proportion of leprosy patients showing lepromatous or mixed lesions is higher in Europeans, Arabs and the penal classes than in the Creole population.

In Cuba a census revealed 2,166 persons suffering from leprosy in 1946. OTEIZA SETIEN *et al* (pp 95, 589) show that the incidence of ambulatory cases varied from 0.163 to 0.6 per 1,000 in different parts of the country, and that the rate in intimate contacts was 33.4 per 1,000. There are 2 special hospitals. Infants born in hospital to diseased parents are separated from them at birth, to be brought up away from infection. IBARRA PÉREZ and GONZÁLEZ PRENDES (p 430) show that the incidence of leprosy in Cuba is in the ratio of 1.52 males to 1 female. In Argentina, FEDERICO GUILLOR and OSVALDO CURCI (p 591) found the proportion of 1.82 male to 1 female leprosy patient, and the predominance of males is generally noted in other countries. They discuss leprosy in women and its relation to pregnancy.

DHARMENDRA and SEN (p 324) give an account of familial and contact spread of leprosy in relation to a family in Calcutta.

MOISER (pp 321-725) is unable to accept the view that long-continued close contact is necessary for the transmission of leprosy, and puts forward once more his opinion that cockroaches are important in transmission. MUÑOZ RIVAS (p 1071) again discusses the possibility that leprosy may be transmitted by fleas. He shows that acid-fast organisms are often present in fleas and their

\*The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1947, v 44. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

larvae in the dwellings of leprosy patients but not (in his experience) in the dwellings of healthy people. Inoculation of triturated fleas which had fed on leprosy patients into monkeys did not give clear-cut evidence. FLOCH and DE LAJUDIE (p. 724) have cultivated acid-fast bacteria from triatomid bugs which had fed on lepromatous thons and from mosquitoes caught in leprosy wards. They do not claim that these were leprosy bacilli.

### *etiology*

COCHRANE, MEXON and PAXDIT (p. 322) have repeatedly injected splenectomized monkeys with material from human leprosy patients. Some of the animals were also fed on *Colocasia esculenta* (which has been thought to predispose to the disease in man) and some were given preliminary injections of Indian ink. Although no dissemination was observed all the animals except those which received the Indian ink tended to develop strongly positive lepromin reactions after the third injection. COCHRANE and RAMANUJAN (p. 327) sum up the results of attempts to infect 38 monkeys with human leprosy material, which were made in the course of 6 years' work. They conclude that a positive lepromin reaction can be obtained only after a primary focus has been established and that *Mycobacterium leprae* cannot parasitize the reticulo-endothelial system unless it multiplies in the corium of the skin and can only develop if the R E system is intact. In tuberculous leprosy the formation of epithelioid foci anchors the bacilli and prevents their dissemination throughout the R E system. But the authors have not been able to produce disseminated leprosy in the monkeys.

HANKS (p. 323) gives the results of attempts to culti- leprosy bacilli in small cubes of leprosy tissue placed in various fluid culture media or on solid media. He used a careful method to assess any increase in the number of bacilli but there was no evidence of multiplication in any experiment. He (p. 721) has carried out tissue-culture experiments with lepromatous tissue and although there was growth of fibroblasts other cells (containing the bacilli) died and there was no evidence of any growth of the bacilli themselves. The same author (p. 722) continued this kind of work, but with tissue from macular and tuberculous lesions. The advancing border of the tuberculous tissue in culture created a stronger impression of viable leprosy bacilli than any other form of leprosy but this was not maintained as the tissue cells proliferated. Fibroblasts from these resistant forms of leprosy rapidly ingested and destroyed bacilli with which they had been infected.

HANKS (p. 722) continued this work by injecting carbon particles into the explanted tissue before culture. He observed that the fate of the bacilli was similar to that of the accompanying carbon particles except that the bacilli were less durable. By doubling the carbon dioxide pressure or by increasing the rate of growth of fibroblasts, the rate of disappearance of the bacilli was increased, and the distribution of leprosy lesions in the body is probably influenced by the same conditions as those which affect the fate of bacilli in cultivated fibroblasts. Internal organs have more, the greater incidence of mitotic cells, more active metabolism and lower pH than cells of the periphery. In work on rat leprosy he (p. 723) has shown that the injection of carbon particles does not influence the dispersal of leprosy bacilli and is good control in experiments on multiplication of organisms. He (p. 724) thinks that the turbidity of plasma surrounding tissue cultures of lepromatous material is not due to increase of the numbers of leprosy bacilli as some investigators have thought but to calcification of the plasma. There is no evidence of multiplication of the bacilli.

The same author (p. 724) infected chick embryos and chick tissue cultures with bacilli from lepromatous nodules but there was no sign of proliferation of the bacilli in any of the experiments.

## Diagnosis Tests

DE SOUZA-ARAUJO (p 1072) describes his method of clamping skin until it is ischaemic, and then puncturing it to obtain lymph for staining in the search for leprosy bacilli. A method for staining leprosy bacilli with Nachtblau (as for tubercle bacilli) is described by HALLBERG (p 591). It is particularly useful for sections. A method for staining the rounded thickenings sometimes seen in leprosy bacilli is described by DE OLIVEIRA CASTRO (p 1072), it is based on the Cooper modification of the Ziehl-Neelsen method. FITE *et al* (p 1008) describe a satisfactory method of staining leprosy bacilli in paraffin sections, using the stain Sudan black B for staining lipid material, that true leprosy bacilli do not contain intracellular material which is stained in this way, but that tubercle bacilli, and acid-fast organisms which have been cultivated from leprosy material, do. This supports the view that these cultivated organisms are not true leprosy bacilli, but are saprophytic.

As a result of a large number of examinations made of recruits in India, McDONALD (p 592) shows that examination of sections of suspected skin lesions can be very helpful in diagnosis. In 80 positive specimens only 1 was lepromatous, the rest were tuberculoid, with only scanty bacilli, but with the typical lesions and epithelioid-cell and round-cell infiltrations, and a few giant cells. Differentiation from skin tuberculosis is not easy and requires expert interpretation of the sections and of the clinical condition, there is no caseation in the leprosy sections and there may be peripheral neuritis with round-cell reaction. Three types of lepromin are used by IGNACIO CHALA and LLERAS RESTREPO (p 823) whole lepromin (which gives a late reaction in tuberculoid leprosy, and sometimes an early reaction), filtered lepromin, and bacillary lepromin. The last is the most active and is recommended for routine work, strongly positive early reactions are given with filtered and anaesthetic nerve leprosy. The culoid leprosy but not in simple macular or anaesthetic nerve leprosy. The preparation of these lepromins is described.

TISSEUIL (p 325) thinks that the lepromin reaction in tuberculoid leprosy, though positive in both diseased and healthy skin, is not specific, because reactions are also produced by injection of other acid-fast bacilli, and because lepromin sometimes gives positive results in healthy persons. The negative reaction in lepromatous disease is due to the fact that all the tissues, even those apparently healthy, contain the bacilli, and this negative result is specific because other acid-fast organisms give positive results.

GARCIA MIRANDA (p 431) states that in non-lepromatous persons, infection with *Mycobacterium tuberculosis* often provokes sensitivity to lepromin as well as to tuberculin. In leprosy patients, however, reactions to these two substances give discordant results. The lepromin test is a gauge of the body's defensive mechanism, and a negative result indicates absence of resistance [see TISSEUIL above]. GINÉS and POLETTI (p 528) similarly state that positive reactors to tuberculin are also positive to lepromin [see also this *Bulletin*, 1943, v 40, 247], and they show that inoculation of BCG may induce a state of reactivity to lepromin, and, perhaps, of resistance to leprosy.

CARBONELL and CONTRERAS DUEÑAS (p 592) compare the histamine skin test, in leprosy, with a test in which a substance (Priscol) is used which acts on the small arteries and arterioles rather than on the capillaries.

## Clinical Findings

The classification of leprosy is discussed by MUIR (p 1073) who recognizes the two characteristic forms, lepromatous and tuberculoid, and the characteristic form which may remain so or which may progress to one of others, or be a stage in transition of one of the characteristic forms to

other or a stage on the way to recovery. Secondary classifications deal with clinical and topographical features, bacteriological findings and the lepromin test.

DAVY (p. 325) holds that in macular leprosy there is a wide range of lesions which shade into each other from the mildest of localized tuberculoid lesions to innumerable poorly-defined macules of lepromatous type without effective localisation. The lepromin test is positive in the mild forms and shades to negative in the severe forms. There seems to be an allergic mechanism in all macular forms, which may appear suddenly.

COCHRANE (p. 1073) thinks that the corium of the skin is the site of active development of leprosy bacilli, and is the area of strategic importance in leprosy. The bacilli in the reticulo-endothelial system are mainly saprophytic. In India many cases of child leprosy are benign and non-progressive and practical consideration need only be given to simple neural leprosy and pre-lepromatous lesions, the latter comprising 5-10 per cent. of all child cases and developing in families in which there is the closest contact with infective patients. The benign cases in children do not require prolonged treatment.

ERMAKOVA (p. 726) shows that there may be injury to the nerves at the root of the tongue in lepromatous leprosy, but that only the sensory nerves are involved.

PARDO-CASTELLO *et al* (p. 1074) state that nerve involvement occurs in lepromatous and tuberculoid leprosy but differs in type in that in the former there is cellular infiltration with masses of bacilli, and in the latter there are thick infiltrations of lymphocytes, epithelioid cells and giant cells, but few bacilli, and caseation sometimes occurs. They therefore think that the so-called neural leprosy belongs to the tuberculoid type. This view is not accepted by some workers.

TISKUL (p. 726) describes the essential characters of tuberculoid leprosy which should not be classified under nerve leprosy.

IGNACIO CHALA (p. 430) has described in detail the skin lesions of tuberculoid leprosy. The account of this work cannot well be abstracted further and the description of the various forms seen should be sought in the original. He makes the point that the lepromin test is positive and that tuberculoid leprosy is not infective and is therefore not a menace to the public health.

DHARMENDRA and SAXENA (p. 324) have studied the course of leprosy in 748 cases observed for 10 years in India. About one-quarter were lepromatous. Definite improvement or complete subsidence occurred in over 40 per cent. of the cases of nerve leprosy.

RADXA (p. 324) describes the progress of a number of untreated cases of early nerve leprosy. Most remained unchanged during several years, but a few improved and more deteriorated. Treatment with Calococcus and sodium glycinate was useful in a group of patients with similar lesions.

BROWN (p. 214) has investigated the blood glutathione in leprosy as an aid to the determination of the state of the oxidation-reduction processes in the patient, and hence of the extent of compensation of the leprosy process.

A description of the eye diseases seen in leprosy is given by MASSARD (p. 213).

Alopecia is not a rare complication of leprosy. It occurred in 84 per cent. of cases in the United States (FAGET p. 593).

MOSE (p. 1074) points out that the lepra reaction is an allergic phenomenon, and therefore presumably is due to a substance allied to histamine. He has tried benadryl, a synthetic anti-histamine substance with considerable success in the treatment of these reactions. POUZAT and ROSS (p. 593) have observed numerous red nodules resembling those of erythema nodosum, in the course of lepra reactions. These are most frequent in lepromatous leprosy. In a

number of cases a definite increase was found in the fasting blood sugar level, and there was evidence of increase of bile pigments in the urine during the reactions. The hyperglycaemia is probably related to the metabolic function of the liver. Treatment of cases of lepra reaction with insulin produced clinical improvement.

### *Treatment*

MUIR (p 824) discusses the treatment of leprosy with the sulphone preparations, quoting his own previously published work and that of the Carville team. The drugs cost £6 per patient per annum [but at Carville the saving in dressings more than compensates for the cost of the drugs, see p 594].

FAGET and his colleagues at Carville (p 594) have issued a report summing up their experience of promin treatment in 177 cases for periods of 1-5 years. The usual course is now to give the drug intravenously 6 days each week for 2 weeks, followed by a rest of 1 week, this cycle is repeated, to give about 207 injections each year. It was necessary to stop treatment in less than 5 per cent because of untoward reactions. This treatment results in improvement in all major chronic manifestations, with bacteriological and histological improvement. MOM (p 594) gives the same doses of promin as are the rule at Carville (2 to 5 gm intravenously each day) but does not allow the same rest periods. His results have been good and have varied with the dosage and length of treatment. He also gives intravenous injections of ascorbic acid each day. He thinks that the use of chaulmoogra as well as promin is an advantage. PEYRI (p 1075) discusses the incidence of leprosy in a province of Mexico. He has treated 30 patients (16 lepromatous, 4 tuberculoid, 10 uncharacteristic) with promin, 2 gm intravenously each day for 6 days each week, with an interval of 15 days every two months. Improvement was seen in all after 200-300 gm had been given. WHARTON (p 326) observed considerable improvement in 7 lepromatous cases treated with intravenous promin.

MUIR (p 327) in England gives diasone by the mouth in a dose of 2.0 gm on each of 3 days each week for 3 weeks, with an interval of 1 week before the course is resumed. This is repeated time after time, and the dose may be pushed to 12 gm a week for 3 weeks each month if there are no reactions. Slight anaemia is treated with iron, liver and yeast. In this way he obtained favourable results in lepromatous leprosy, which had not been possible with chaulmoogra alone. FERNANDEZ and CARBONI (p 595) have had considerable success with diasone given by mouth in tablets containing one-third of a gramme each. The daily dose best tolerated is 2 gm for 8 weeks, followed by a rest of 3-4 weeks, and repeated. Intolerance may be noted after 2 weeks, but usually disappears if the drug is temporarily stopped, and there may be methaemoglobinaemia and anaemia which usually responds to anti-anaemia treatment. In lepromatous leprosy there is often marked improvement, with softening of the nodules and reduction in size.

FAGET, POGGE and JOHANSEN (p 326) record some considerable benefit in 7 patients with advanced lepromata treated for 1 year with promizole. The same authors (p 326) show that in 104 patients treated with diasone by mouth, and observed up to 2½ years, about one-quarter became bacteriologically negative and two-thirds showed improvement. It was necessary to discontinue treatment in a quarter of the patients, for various reasons, but in the rest the drug was well tolerated. The daily dose was gradually increased from 0.3 gm to 1.0 gm for adults.

FAGET (p 727) sums up his experiences with promin, diasone and promizole, the results of which have been very similar. The active principle of them all is apparently the diamino-diphenyl sulphone. Improvement was noted in almost all cases within 3 years, often in a much shorter period.

In an account of the work done under most difficult conditions at the large leprosy hospital in Malaya during the years of Japanese occupation RYU (p. 720) remarks that the lack of *Mycobacterium* oil convinced him of its value. HEATHCOTE *et al.* (p. 777) discuss the methods of treatment (largely with neutralized chaulmoogra oils) and prevention (agricultural colonies for infective patients) used in the French colonies. BAKER (p. 908) notes the chaulmoogra oil irritates the stomach but he has given it in dogs and in man by duodenal tube and has satisfied himself that it is effectively absorbed.

Penicillin is apparently useless in leprosy (FIGUEROA and DEAN, PANAMA, p. 214).

REINSTEIN (p. 728) states that electrophoretic analysis of his anti-leprosy serum shows that it contains more gamma globulin than normal serum and this he thinks is due to the presence of antibodies. The serum was prepared against an acid-fast bacillus cultivated from a patient with leprosy and regarded by the author as the cause of the disease (though many other leprologists would probably not accept it).

Improvement was observed in a number of cases of nerve leprosy treated by FIGUEROA and DEAN (p. 14) with intravenous methylene blue.

Good results in the treatment of leprosy ulcers were achieved by LANGSTON (p. 596) who used Tisearil's method of intramuscular injections of acetylcholine hydrochloride.

MOSE and BERXAL (p. 596) have used a weak solution of tyrothricin as a preparation for leprosy ulcers, with great success. 14 of 15 healed though they had resisted other treatments.

### Control

MACKAY (p. 720) shows that at the Makete leprosy settlement in Tanganyika Territory there are about 1,500 inmates. Each patient has not less than 5 acres of land and can therefore become self supporting. Admission is voluntary and there is rarely need to separate husbands and wives because conjugal infection is rare. The incidence of leprosy in the children is also surprisingly low. In Central Africa only 5-10 per cent. of cases are lepromatous.

AUSTIN (p. 723) defends the system of compulsory segregation of leprosy patients in the scattered islands of Fiji where a voluntary system would not enable earlier cases to be found and treated. ROBERTS agrees that it is evidently a procedure suitable to those conditions, but condemns for Asia and Africa where the bulk of cases occur the indiscriminate compulsory isolation of all types of leprosy including the large numbers of non-infective nerve cases.

The problem of home isolation of leprosy patients in the Philippines is discussed in the *International Journal of Leprosy* (p. 377). Under the existing law only bacteriologically positive patients are isolated in institutions; negative patients are placed on parole. In the opinion of some of the members of the staff of the public health department home isolation is likely to fail and it would be unwise to relax the regulation in so highly endemic an area as the Philippines.

FUGET (p. 588) contributes a history of the National Leprosarium, Carville, U.S.A., where much work on treatment with primum and diaseone has recently been done. In 51 years only one attendant has developed the disease.

CHALA (p. 597) describes the leprosy institutions of Colombia, where there are 3 large leprosia and 11 dispensaries.

Charles W. Francis



## RABIES

REMLINGER, P & BAILLY, J La rage et le traitement antirabique pendant  
ces vingt dernières années [Rabies and Anti-Rabies Treatment during  
the Last Twenty Years] Biol Méd 1948, June-July-Aug, v 37,  
Nos 6-7-8, 101-28 [247 refs]

In this exceedingly informative article the authors review the most important work published on rabies and on its specific treatment during the past 20 years. The following paragraphs summarize the points on which emphasis is laid.

The causal agent of rabies is a virulent substance of a protein nature. Endowed with powers of assimilation, it is capable of cultivation, particularly on the chorio-allantoic membrane of the chick embryo.

The Viverridae (civet family) in South Africa, Desmodidae (vampire bats) in Paraguay, Argentine and British West Indies, and skunks in the United States have to be added to the list of animals that transmit the infection in nature.

In West Africa, Equatorial Africa and in tropical countries generally, rabies and rabies virus behave exactly as in temperate regions.

The rabies virus occurs not only in the nervous system and salivary glands but also, owing to its central and peripheral nervous distribution, in almost every organ. It has been demonstrated in the suprarenals, spleen, liver, kidney, lung, testicle, Harder's gland, retina, choroid, vitreous body and crystalline lens, but not in the aqueous humour.

The Swiss mouse (preferably) and the white mouse are, in the opinion of many, animals of choice for experimental work on rabies. The former, ten times more susceptible to rabies virus than the rabbit or guinea-pig, is incomparable for assessment of the immunizing power of different anti-rabies vaccines (WEBSTER).

The "singleness" of street virus contrasts with the "plurality" of fixed virus—a virus "fixed" only in name. Fixed viruses differ among themselves more than street viruses, on repeated "passage" the former become more and more sensitive to the action of desiccation and of glycerin, less and less to that of dilution and of ether. Anti-rabies institutes should have subjected to periodic control the strains of fixed virus used in the preparation of their vaccines. Desiccation does not attenuate, it preserves the rabies virus. Attenuation of the virus in cords suspended in Pasteur flasks is achieved by proteolysis.

In almost every country the classical method of Pasteur and the dilution method of Hognes have been replaced by the use of etherized and, especially, phenolized vaccines, which retain their immunizing properties for months, can be despatched to places far from their place of manufacture and with which immunization can be effected in hospitals, dispensaries or even in the houses of the physician or of the bitten person.

Anti-rabies serum has failed in practice to fulfil the hopes to which it originally gave rise.

By reason perhaps, of the period of "neurotropism", through which we are now passing, the number of paralytic accidents complicating anti-rabies treatment is on the increase. In this connexion it is important to distinguish between "*rage de laboratoire*", where the virus used in treatment is recovered on autopsy, and the rightly termed "paralytic accidents" which, though usually less serious, are much more frequent.

Failures of treatment should not be concealed any more than the neuro-paralytic accidents of treatment. Often they result from an inadequate amount of vaccine employed. Blame must be laid not on Pasteurian treatment

## MALARIA

WORLD HEALTH ORGANIZATION INTERIM COMMISSION Expert Committee on Malaria. Report of Second Session. Washington, D.C. May 18-25, 1948. 50 mimeographed pp. [W.H.O. IC/205. W.H.O. IC/Mal 25 8 June 1948.]

The report of this session of the W.H.O. Expert Committee on Malaria is important as would be expected. The members were GABALLON CUYLL, RUSSELL, VAUGHAN VISWANATHAN and PAMPANA assisted by AFRIDI FIELD Bagster WILSON AYKROYD ALVARADO ASTALES VARGAS COATSAY HILF SOFER and STAGG.

The report is divided into 10 sections, the first of which is an introduction and the second a very brief statement on world needs. Section 3 deals with W.H.O. malaria policy which is to assist governments to accomplish effective malaria control through W.H.O. regional organizations. It is concerned with programmes and machinery for control training the spreading of knowledge the development of uniform procedure and nomenclature and the promotion of measures to protect countries against the introduction of anophelines from the outside.

Examples are given of different existing antimalarial organizations such as those established in India and certain South American countries the emphasis being on elasticity. Training involves instruction of three grades of staff—directive professional staff, assistant professional staff and subordinate personnel—and it includes the means for making available to them the latest information from all over the world. Individual experts and operational demonstration teams should primarily demonstrate the use of residual insecticide spraying as a method of malaria control. Three teams should be formed as early as possible to be allocated, on request to Central Africa, South-East Asia and Tropical America.

The general public must be educated but the most effective propaganda is successful demonstration of practical malaria control.

In section 4 on Agriculture and Malaria there is a provisional memorandum prepared by the F.A.O. in which are discussed such matters as the effects on agricultural production of ill health due to malaria and the possibility that malaria may be introduced into an area as a result of change of human or natural agencies for instance migration (possibility which may also apply to *schistosomiasis*).

Section 5 is devoted to the use of insecticides. Of which DDT is the most satisfactory. Benzene hexachloride has a shorter residual action and a disagreeable odour. DDD and TDE (1 trachloro-diphenylethane) are useful larvicides where the safety of fish needs consideration. chlordane and chlorinated camphene do not possess as long an effective residual action as DDT. combinations of pyrethrins with pyrethrin compounds increase the effectiveness of the pyrethrins, but need more investigation. parathion is toxic for warm-blooded animals.

The committee expresses the opinion that there is definite and overwhelming evidence that modern insecticides properly applied can be relied upon to produce a significant reduction in malaria morbidity though doubt has been expressed in Africa as to the efficacy of DDT in *Anopheles gambiae* and more work is needed.

The effective dose of DDT used as a residual spray against adult anophelines varies in different circumstances from 60 to 200 mgm per square foot, and the optimum frequency of spraying is once in 8 weeks to once in 12 months. Many factors must be taken into account including the composition of the surface to be sprayed, and the habit of the mosquitoes concerned, before

## Malaria

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rules can satisfactorily be laid down for any particular work As larvicides the new compounds are very effective, and for DDT the effective dose is 6 quarts of a one per cent solution in kerosene or fuel oil per acre of stagnant water, and one part of DDT per million of water in running streams Details are given of other formulations In rural communities residual-spray-killing of adult anophelines is usually more economical than the use of larvicides, but this may not be so in urban centres For species which rest indoors, residual spray may be enough, but for those which tend to rest outside, after feeding indoors, anti-larval methods are needed also

In section 6, on chemotherapeutics in malaria control, the committee accepts the proposition that in the existing state of knowledge measures against mosquito transmission are the only methods giving permanent control of malaria, but agree that chemotherapy and chemoprophylaxis are important in the clinical control of epidemic malaria, and that the latter, though secondary, is important for personal protection Suppressive drugs are particularly useful for collections of workmen, for armies in the field, and for certain other groups

Further information is needed on the results of taking synthetic drugs for many years, and on their effect on the state of immunity of people living in highly endemic conditions

The various drugs in common use are discussed in some detail, and courses commonly used in treatment are quoted, for instance —

## Mepacrine

	1st day	2nd day	Succeeding days	Total
Non-immunes	1.0	0.3	0.3 × 5 days	2.8 gm
	0.9	0.6	0.3 × 5	3.0 "
	0.6	0.6	0.3 × 5	2.7 "
Partial immunes	0.6	0.3	0.3 × 3	1.8 "

These amounts are for adults and are administered in three or more daily doses

The optimum suppressive dose for non-immunes is 0.1 gm daily, a preliminary build-up of 0.3 gm daily for five days is sometimes advocated

## Chloroquine

American experience indicates that the optimal adult dosage, expressed as base is as follows —

	1st day	Succeeding days	Total
U.S.A.	0.6 gm (divided in two doses)	0.3 gm daily for three days	1.5 gm
Venezuela	0.9 gm (divided in three doses)	0.9 gm on second day only in three doses	1.8 gm

N.B. — The tablets of 0.25 gm of chloroquine diphosphate contain 0.155 gm of base. For suppression 0.3 gm. of base (0.5 gm of chloroquine diphosphate) is given once each week.

*Paludrine*

There is such wide difference in the effective range of dosage that the indications which follow must be regarded as provisional.

- (a) For standard therapy in adults paludrine monohydrochloride 0.3 gm. daily for five to ten days (the monohydrochloride contains 88.5 per cent. of paludrine base).
- (b) For single dose therapy in adults 0.3 gm. of monohydrochloride in one dose, followed by a weekly suppressive dose of 0.1 gm. to 0.3 gm. on the same day of the week.

The single dose method is not recommended for routine hospital treatment of *P. falciparum* malaria with paludrine. The committee notes that the best results with paludrine as a preventive have been obtained in the Far East, where 0.3 gm. given on one day each week may be enough, but in other parts of the world, and with other strains of *P. falciparum* this dosage may be insufficient [a daily dose of 0.1 gm. has, in fact, been advocated in West Africa, see WALLS, below].

The gametocides plasmoquine, pentaquine and (eo)-pentaquine are considered briefly.

In section 7 on research, a number of examples are given of studies which need to be undertaken either as basic research or as applied research. These examples are not discussed, and should be sought in the original by those proposing to initiate research.

Section 8 is concerned with quarantine especially with regulations for the disinsection of ships and aircraft which may introduce anophelines into countries which the authorities desire to protect: this section should be read in the original.

Sections 9 and 10 deal with recommended resolutions, and with conclusions and recommendations.

[The report as a whole represents a careful essay on some aspects of malaria control, which should be closely studied by governments and medical organizations in the tropics. A basic assumption is made that malaria causes ill-health, without much differentiation between the disability experienced in conditions of seasonal transmission and in those of perennial transmission with a resulting high degree of immunity in adults. The extent of malarial illness in the indigenous people of countries showing these degrees of transmission is not yet fully understood (and the Committee suggests research on the subject) and the effect of the various methods of control on communities subject to hyperendemic conditions is not satisfactorily known. Obviously if control is perfect and permanent, there would be no malaria, but partial control only is possible in many places and this may produce unexpected results. It would seem necessary that a long term observation should be carried out to attempt to assess the health importance of malaria in the various conditions of transmission, and of the effects of partial control in hyperendemic areas. The committee lays great stress on residual insecticides, and little stress on the older methods of drainage, water-control, biological control, etc. but it may be possible as the committee admits that races of anophelines not so susceptible to the action of insecticides (though none has yet been found) or having resting habits which do not bring them into contact with pyrethroid surfaces will be selected out, to replace those which now transmit the disease. It would be unwise to lose sight of the well-tried methods and the committee has probably no intention of doing so.

Charles H. Woods

\*ALVING, A S, CRAIGE, B, Jr, PULLMAN, T N, WHORTON, C M, JONES, R, Jr & EICHELBERGER, Lillian Procedures used at Stateville Penitentiary for the Testing of Potential Antimalarial Agents *J Clin Investigation* 1948, May, v. 27, No 3, Pt 2, 2-5

About 500 inmates of the Illinois State Penitentiary at Stateville volunteered to act as subjects for the controlled clinical testing of new antimalarial drugs. The results of studies already completed are set out in this special malaria supplement of the *Journal of Clinical Investigation*. The primary object of the studies was to obtain information about the effect of potential antimalarial drugs upon the relapse rate of sporozoite-induced *P vivax* malaria. The prophylactic and suppressive effects of the drugs were also studied, and observations were made on their toxicology and pharmacology.

All the subjects were white males in good physical health between the ages of 21 and 40, none had lived in a known malarious area and none had a history suggestive of previous malaria infection. There is no endemic malaria in Stateville. The Chesson strain (New Guinea) of *P vivax* malaria was used. This strain is characterized by a high relapse rate when such drugs as quinine or mepacrine are used in treatment, and by the almost complete absence of delayed primary attacks.

*Anopheles quadrimaculatus* was used for the transmission of infection. Each patient received the bites of ten infected mosquitoes. In the standard prophylactic procedure the drug to be tested was administered on the day before infection, on the day of infection, and on each of the following six days. Thick films of the peripheral blood were taken daily after the eighth day following inoculation.

In the curative tests the drugs were administered at intervals of four hours to obtain fairly constant concentrations in the body fluids. Slowly excreted drugs such as quinacrine, chloroquine and SN-8617 were given less frequently. The usual period of drug administration was 14 days.

Most of the drugs tested were members of the 8-aminoquinoline group of compounds for these the usual observations of temperature, blood pressure, urine analysis, and plasma drug concentrations, were supplemented by a leucocyte count every day and a differential count every fourth day, haemoglobin and methaemoglobin determination every day, and electrocardiogram after treatment.

Norman White

JONES, R, Jr, CRAIGE, B, Jr, ALVING, A S, WHORTON, C M, PULLMAN, T N & EICHELBERGER, Lillian A Study of the Prophylactic Effectiveness of several 8-Aminoquinolines in Sporozoite-Induced *Vivax* Malaria (Chesson Strain) *J Clin Investigation* 1948, May, v 27, No 3, Pt 2, 6-11 [18 refs]

The four compounds studied, pamaquin SN-11,191, SN-1,452 and SN-13,276 (pentaquine) are all 6-methoxy-8-aminoquinolines. They all have high antimalarial activity in avian infections and their toxicity in the monkey is low. The methods of infection and drug administration are described above. Pamaquin 90 mgm [Pamaquin base] a day for 8 days beginning the day before inoculation protected two of five patients from infection, they exhibited no sign of malaria during 20 months of observation. Two developed fever and parasitaemia 18 and 19 days after sporozoite inoculation. One developed a delayed primary attack of malaria 106 days after infection.

\*This and the following 21 abstracts represent summaries of a symposium on malaria which occupied a complete number of the relevant journal. They are therefore presented together, in the order in which they appeared.

Two of three subjects treated with SN 11 191 (90 mgm. a day) and two treated with SN 1 452 (240 mgm. a day) had no malaria during 20 months of observation. One subject in each of these two groups developed malaria within 3 weeks of inoculation.

The four subjects who served as controls for these first three drugs tested developed clinical malaria 12 to 14 days after inoculation.

One of five subjects treated with pentaquine (120 mgm. a day) developed fever and parasitaemia 22 days after inoculation. The other four have shown no evidence of malaria during 9 to 11 months of observation. The 12 control subjects for this experiment all developed clinical malaria in 12 to 19 days.

All of 8 patients receiving 180 mgm. of pentaquine a day remained free from malaria during nine months of observation although two of them received the drug for only two days and two others for only three days after the day of inoculation. The ten controls for this experiment all developed malaria 12 to 17 days after inoculation.

All doses mentioned above are in terms of base weight.

As the drugs were used in doses approaching the estimated maximum tolerated dose signs of toxicity were expected and found. Epigastric discomfort or pain (most severe in patients taking 180 mgm. SN 13,276) anorexia, nausea and vomiting were noted. Cyanosis was noted when the methaemoglobin exceeded 6 or 7 per cent. of the total haemoglobin. The average loss of haemoglobin was 1.75 gm. per 100 ml. of blood the greatest loss being about the 12th to 14th day after the start of medication.

The results show that all four drugs may act as true prophylactics for sporozoite-induced *P. vivax* malaria, but they did not protect all subjects. There was no positive correlation between plasma drug concentration and the prophylactic effect of these drugs. In subjects whose primary attacks of malaria were not prevented, the disease was so altered by the prophylactic treatment that it was rendered susceptible to cure by drugs ordinarily incapable of preventing relapse. It would seem that these drugs exert a deleterious effect upon pre-erythrocytic stages of the malaria parasite. Their relatively high toxicity precludes their general use as prophylactics. Norman H. White

PETLIMAN T. V. ECKELBERGER, Lillian, ALVING A. S., JOHNS R., JR. CRACK, B. JR. & WHORTON C. M. The Use of SN-10,275 in the Prophylaxis and Treatment of Sporozoite-Induced *P. vivax* Malaria (Chesson Strain). *J. Clin. Investigation*. 1948 May v 27 No. 3 Pt. 2, 1716, 3 figs. [14 refs.]

SN 10,275 is 6,8-dichloro-2-phenyl-1-piperidyl-4-quinolinemethanol and has a close chemical similarity to quinine. Three subjects receiving 0.859 gm. (of base) a day for 8 days beginning the day prior to inoculation developed fever and parasitaemia, but the prepatent periods were from 6 to 9 times longer than in three control subjects. The plasma concentrations at the time of appearance of parasitaemia ranged from 68 to 110 gamma per litre.

After treatment with SN 10,275 the latent periods of those who relapsed were 20, 107 and 99 days. The median latent periods observed with quinine and quinacrine in the Chesson strain of malaria under the conditions of this investigation were 15 and 31 days respectively.

SN 10,275 remained in the plasma for long periods after medication was stopped. There was a wide variation in the rate of fall: the mean loss for the majority of the group was 20 per cent. per week, a much lower rate of disappearance than that shown by quinine or quinacrine in mepacrine.

Eight patients received SN 10,275 at a dosage of 1.0 gm. of the salt a day. One had mild gastro-intestinal symptoms: cramps, nausea and mild diarrhoea.

Another had fever of 102°F, headache and backache at the end of the 14-day course of treatment. All eight patients had photosensitivity of the skin, from a slight tingling of the face to severe burning sensations with erythema. One had some desquamation of the skin of the nose and another mild labial oedema. These symptoms appeared only after exposure to sunlight. The severity and duration of these symptoms are roughly correlated with the mean concentration of SN-10,275 in the plasma.

Toxic reactions and the variation in the rate of disappearance of the drug from the body limit the value of SN-10,275 as a suppressive drug, but further investigation of related compounds is indicated because a non-toxic drug with the antimalaria activity of SN-10,275 which remained in the body for long periods of time would have great value in the suppression of malaria.

Norman White

CRAIGE, B. Jr, EICHELBERGER, Lillian, JONES, R. Jr, ALVING, A. S., PULLMAN, T. N. & WHORTON, C. M. The Toxicity of Large Doses of Pentaquine (SN-13,276), a New Antimalarial Drug. *J Clin Investigation* 1948, May, v 27, No 3, Pt 2, 17-24, 4 figs [16 refs]

The purpose of the observations reported in this paper was to define the margin of safety of pentaquine (SN-13,276) in the treatment of malaria. In the therapeutic trials, five subjects received 120 mgm pentaquine base a day with quinine for 14 days. Five others received similar treatment but without quinine. In the prophylactic trials, five subjects received 120 mgm pentaquine base a day for eight days, and five 180 mgm a day for eight days. The doses used were double or treble the amounts necessary for antimalarial treatment.

The toxic reactions were severe. Most of the subjects had severe abdominal pain, nausea, anorexia and methaemoglobinaemia, similar to the symptoms produced by toxic doses of pamaquin. Serious physiological abnormalities developed in three of the subjects taking 120 mgm of pentaquine a day without quinine, therapeutically. They displayed postural hypotension with syncope, arterial and venous oxygen unsaturation, and loss of weight, which persisted for a long time after the end of treatment. The symptoms were possibly due to central impairment of the sympathetic nervous system.

Norman White

ALVING, A. S., CRAIGE, B. Jr, JONES, R. Jr, WHORTON, C. M., PULLMAN, T. N. & EICHELBERGER, Lillian. Pentaquine (SN-13,276), a Therapeutic Agent effective in reducing the Relapse Rate in Vivax Malaria. *J Clin Investigation* 1948, May, v 27 No 3, Pt 2, 25-33, 2 figs [14 refs]

The procedure adopted at the Illinois State Penitentiary for the testing of antimalarial drugs has been described above. In spite of efforts to secure uniformity in the induced disease variations occurred. It was possible, however, to distinguish severe from less severe infections according to the length of the prepatent or preceding latent periods. Subjects with long prepatent or latent periods had a relapse rate of 67 per cent after treatment with so-called suppressive drugs. Those with short periods a relapse rate of 98 per cent. A small group of volunteers had massive infections, being bitten by 80 infected mosquitoes instead of the ten used in the standard procedure. Their relapse rate was 100 per cent. The subjects were accordingly divided into three categories representing a moderate a severe and an extremely severe challenge to the therapeutic efficiency of the test drug.

Pentaquine was given to 82 persons in daily doses of 60 mgm. of base or less for 14 days. When it was given alone in doses of 30 or 60 mgm. a day fever disappeared in two to four days parasites disappeared in three to six days. Twenty-six moderately infected subjects were given 60 mgm. a day and four others 30 or 45 mgm. a day. These 30 subjects also received 2 gm. quinine sulphate daily. The relapse rate was only 3 per cent as compared with 67 per cent obtained when similar cases are treated with suppressive drugs. Of 1 subjects with severe infections treated with pentaquine alone in doses of 15 to 45 mgm. of base a day all but one relapsed. Pentaquine 60 mgm. a day reduced the relapse rate of severely infected patients only two of four relapsed. Seventeen severely infected subjects received this daily dose of pentaquine with 2 gm. quinine sulphate, for fourteen days only three relapsed—a reduction in the relapse rate from 88 to 18 per cent. The extremely heavy infections all relapsed after pentaquine treatment.

Pentaquine should only be administered under close medical supervision. The daily dose of 60 mgm. should not be exceeded this has the same toxicity as 30 mgm. of pamaquin base or 67 mgm. of its naphthoate salt. The toxicity of pentaquine is too great to warrant its use in prophylaxis or prolonged suppression.

Norman White

ALVIN A. S. PILLMAN T. W., CRAIG B. JR JONES R. JR WHORTON C. M. & EICHELBERGER, Lillian. The Clinical Trial of Eighteen Analogues of Pamaquin (Plasmochin) in *Vivax* Malaria (Chesson Strain). *J. Clin. Investigation*. 1948 May v 27 No. 3, Pt. 2, 34-45 4 figs. [25 refs.]

This is a record of work done in the search for a drug possessing the capacity of pamaquin to reduce the relapse rate of *vivax* malaria, but devoid of the toxic properties of that drug which hamper its extended use. The observations were made in the Illinois State Penitentiary the procedure adopted is described above. Only pamaquin analogues with pamaquin-type toxicity in animals were used. They had previously been tested for antimalarial activity in avian infections and for toxicity in rodents, dogs and monkeys.

The eighteen 8-aminoquinolines tested were SN 191 SN 9,972, SN 11 191 SN 12,325 SN 12,352 SN 12,354 SN 12,451 SN 12,522, SN 12,523 SN 13,274 SN 13,276 SN 13,280 SN 13,429 SN 13,619 SN 13,694 SN 13,697 SN-14 011 and DR 15,302. It was at first planned to administer the maximum tolerated dose as estimated from the animal experiments. Severe toxic reactions caused by four of these drugs at this high dosage led to the abandonment of this plan. Thereafter of the estimated maximum tolerated dose was administered if toxicity for man was found to be absent, or mild, larger doses were tried.

Drugs were administered in equal doses every four hours over a period of fourteen days. Quinine was administered concurrently with the drugs, 2 gm. of the sulphate or dihydrochloride daily.

Eight of the drugs were ineffective in preventing relapse of severe infections in the doses used. Ten compounds apparently cured one or more patients with severe infections. Five exhibited pronounced activity inasmuch as the majority of patients treated with them had not subsequently relapsed (follow-up period from two months to one year). These drugs are SN 9,972, SN 13,274 SN 13,429 DR 15,302 and SN 13,276 (pentaquine).

No serious toxic symptoms were caused by any of the drugs on the reduced dosage the most common symptoms were abdominal pain, nausea and vomiting. Cyanosis occurred when methaemoglobinuria exceeded 5 or 6 per cent of total haemoglobin. Mild drug fever leucocytosis and leucopenia have been observed.



The studies indicate that the curative properties of pamaquin are shared by several analogues, but no definite conclusions can be drawn as to the specific molecular configuration required in a curative drug

Drug régimes which produced a high percentage of cures tended to prolong the subsequent latent periods in patients whom they failed to cure

Norman White

PULLMAN, T N, CRAIGE, B, Jr, ALVING, A S, WHORTON, C M, JONES, R, Jr, & EICHELBERGER, Lillian Comparison of Chloroquine, Quinacrine (Atabrine), and Quinine in the Treatment of Acute Attacks of Sporozoite-induced Vivax Malaria (Chesson Strain) Preliminary Report *J Clin Investigation* 1948, May, v 27, No 3, Pt 2, 46-50, 2 figs [15 refs]

The antimalarial chloroquine (7-chloro-4-(4-diethylamino-1-methyl-butyl-amino)-quinoline) was synthesized during the late war in USA. Its activity was reported on by LOEB *et al* [this *Bulletin*, 1946, v 43, 708], and has now been compared with that of quinine and quinacrine (atebrin, mepacrine), under controlled conditions, in the treatment of primary attacks and early relapses of sporozoite-induced *P vivax* malaria of S Pacific origin (Chesson strain). For this purpose, 39 prisoner-volunteers were infected by the bites of 10 *Anopheles quadrimaculatus* or by injection of sporozoites from their salivary glands. Treatment was begun early in the attacks. On the first day, 0.8 gm chloroquine base was given, followed by 0.2 gm daily for 6 days (total 2.0 gm over one week). In the same period approximately 2.7 gm atabrine base and 11 to 12 gm quinine base were administered (or 21 to 23 gm of quinine base over 14 days) to different groups. The dosage approached the maximum which was well tolerated. Plasma levels of each drug were measured by the methods of BRODIE & UDENFRIEND [this *Bulletin*, 1943, v 40, 821 1944, v 41, 453, 1947, v 44, 793].

Parasites were generally removed from the blood most rapidly by chloroquine. The relapse rate for each drug was 90 per cent or over. The latent interval after drug administration was longest after chloroquine treatment, possibly owing to its slower excretion or degradation, or to the greater margin between minimal effective plasma level and that reached by the above dosage. The drug proved superior to quinine and atabrine under the conditions employed.

J D Fulton

JONES, R, Jr, PULLMAN, T N, WHORTON, C M, CRAIGE, B, Jr, ALVING, A S & EICHELBERGER, Lillian The Therapeutic Effectiveness of Large Doses of Paludrine in Acute Attacks of Sporozoite-induced Vivax Malaria (Chesson Strain) *J Clin Investigation* 1948, May, v 27, No 3, Pt 2, 51-5, 2 figs [17 refs]

Reports on the treatment of *P vivax* and *P falciparum* infections with paludrine have been reviewed [this *Bulletin*, 1946, v 43, 402, 821, 1947, v 44, 282, 1948, v 45, 34, 238, 491]. Its value in treatment of acute attacks following sporozoite-induced infections of *P vivax* of S W Pacific origin (Chesson strain, which is characterized by early onset of primary attacks, high relapse rate and short interval between attacks) has been compared with that of other suppressive drugs. The patients were healthy white prisoner-volunteers and were infected by the bites of 10 *A quadrimaculatus* or by injection of their salivary glands. Only primary attacks or early relapses were treated so as to avoid the factor of acquired immunity, and treatment was begun at the onset of fever or detection of parasitaemia. All drugs were given by mouth, and the dosage recorded represents that of the free base. Ten

patients were treated with paludrine and received 0.97 gm. daily for 14 days in equal doses given every four hours. The dosage for quinacrine (atebun, mepacrine) was 0.87 gm. in four equal doses on the first day and 0.33 gm. similarly divided on the following 6 days. Pentaquine (6 methoxy-8(5 isopropylaminoamylamino)-quinoline) was given in 10 mgm. doses every 4 hours for 14 days. The method of SPIXAS & TORTIV [this *Bulletin* 1946 v 43 207] was used for estimation of paludrine in plasma and one based on that of BLANCHET *et al.* [this *Bulletin* 1947 v 44 783] for pentaquine.

Quinacrine was more effective in terminating acute attacks than paludrine which cleared the blood of parasites less slowly than chloroquine (see above). When infections were severe radical cures were not obtained with these drugs, but paludrine was a valuable drug in treatment of acute infections, and its side effects were negligible. Some patients with less severe infections did not relapse after treatment with it or with quinine. The length of the latent period after treatment with paludrine was intermediate between that after treatment with quinine and atebun. Neither quinoline nor pentaquine exhibited synergistic activity with paludrine.

J. D. Fulton

LIVING A. S. EICHELBERGER, Lillian CRAIG B. Jr. JONES R. Jr. WHORTON C. M. & PULLMAN T. V. Studies on the Chronic Toxicity of Chloroquine (58-7618). *J. Clin. Investigation*, 1948, May v 27 No. 3, Pt. 2, 60-63 4 figs. [16 refs.]

These studies were undertaken to determine whether chloroquine could be taken for long periods as a malaria suppressive without causing serious toxicity. To establish the margin of safety larger doses than those necessary for suppression were given. The subjects were inmates of the Illinois State Penitentiary free from any physical disability or neurosis. There were two groups of twenty each. The members of the first group each received 0.5 gm. chloroquine base once a week for a year. Members of the second group were given 0.3 gm. of the base daily in two doses for 77 days, and then 0.5 gm. weekly as in the first group for the rest of the year. In the daily dosage studies, mean low plasma concentrations in excess of 200 gamma per litre were maintained for ten weeks. A plasma chloroquine concentration of 10 gamma per litre is sufficient for malaria suppression. Individual low values in excess of 500 gamma per litre occurred without unusual symptoms.

On the higher dosage usual disturbances headache bleaching of the hair electrocardiographic changes and slight loss of weight occurred. These symptoms are said to have caused no incapacity and they diminished or disappeared when the dose was reduced. Member of the group on the weekly dose suffered from occasional headaches and lost little weight. Two had a skin eruption resembling lichen planus.

It is concluded that chloroquine is a safe antimalarial preparation when given in the recommended dosage. The dosage recommended for the treatment of an acute attack of a *tert* or *quarta* form of malaria is 1.5 gm. of chloroquine base in three days for suppression 0.3 gm. weekly.

Norman White

SHANNO J. A. EARLE D. P. Jr. BERRILL R. W. & TUCKER J. V. Studies on the Chemotherapy of the Human Malaria. I. Method for the Quantitative Assay of Suppressive Antimalarial Action in Virax Malaria. *J. Clin. Investigation*, 1948 May v 27 No. 3 Pt. 2, 64-74 4 figs.

It has now been demonstrated by SHANNO and CRAWFORD (this *Bulletin* 1948, v 45 62) that in *per zoster*-induced *P. vivax* malaria and in infection with *P. cynomolgi* in monkeys tissue phase of the infection occurs. From the

persistent tissue phase erythrocytic forms may arise and thus bring about relapses. This tissue phase is absent in blood-induced infections and relapses do not occur. The activity of drugs has been classified as prophylactic, suppressive or curative, depending on the effects produced. The practical needs of war created a demand for active suppressive agents, and for assessment of their value blood-induced infections were widely used. The authors have investigated the validity of this procedure and have tested the susceptibility to quinine of the red cell forms which arise from inoculation of infected blood as well as from sporozoite inoculation. The susceptibility of different strains of the same plasmodium to this drug was also investigated. For this purpose standardization of conditions with regard to host and parasite were necessary in order to obtain reliable results.

White syphilitic patients with central nervous system involvement, having no previous history of malaria and therefore presumed to be susceptible, were employed. In the earlier experiments, the McCoy strain of *P. vivax* was used and its biological characters are described. Thirty patients were inoculated with 500,000 parasites from an early primary infection and the course of parasitaemia was followed in blood smears. Therapy was started on the fourth or fifth day of fever and drug dosage was arranged to give a constant plasma level for 4 days. Estimations were made by the method of BRODIE & UDENFRIEND [this *Bulletin*, 1943 v 40, 821]. If blood smears became negative as the result of treatment, observation was continued over a period of 14 days, and if still negative reinoculation with twice the original number of parasites was carried out and observation continued for another period of 14 days.

The results of therapeutic treatment could be arranged into three classes. In the first, the drug was without effect, in the second a temporary effect was obtained with partial or complete disappearance of parasitaemia and fever, followed by recurrence within a specified period. In the third class, there was complete disappearance of parasites and the patient became susceptible to inoculation. The three classes were correlated with mean quinine plasma concentrations, indicating "that the susceptibility to quinine is a stable characteristic of the infective organism." The correlation between plasma-quinine levels and therapeutic effect was greater than between oral dosage and effect. The result obtained with a given drug concentration was independent of the degree of parasitaemia. Those obtained by similar treatment of 15 patients infected with the same strain of parasite by means of sporozoites indicated that the action of quinine against the resulting blood forms did not differ from its action against the same forms derived from blood inoculation. In similar experiments the Chesson strain of *vivax* malaria of New Guinea origin appeared to possess greater resistance to quinine than the McCoy strain. Certain characters of the Chesson strain are of special value in blood-induced infections for indicating the resistance of red cell forms to chemotherapeutic agents [This important paper should be consulted in the original by those interested.]

J D Fulton

EARLE D P, Jr, BERLINER, R W, TAGGART, J V, WELCH, W J, ZUBROD, C G, WISE, Nancy B, CHALMERS, T C, GREIF, R L & SHANNON, J A  
Studies on the Chemotherapy of the Human Malarias II Method for the Quantitative Assay of Suppressive Antimalaria Action in Falciparum Malaria *J Clin Investigation* 1948, May, v 27, No 3, Pt 2 75-9

In continuation of the work described in Part I of the series dealing with *P. vivax* [above], the susceptibility of the erythrocytic forms of 2 strains of *P. falciparum* to quinine has now been investigated as a basis for the assessment

of antimalarial activity. Similar studies projected for *P. malariae* had to be abandoned on account of practical difficulties. The patients as before were neurosyphilitics carefully chosen, and received an intravenous inoculation of 500,000 erythrocytic forms of the potentially virulent McLendon strain of *P. falciparum* from an untreated patient on the first or second day of fever and the course of the infection was followed in blood smears. Therapy was begun early in the infection to avoid danger to life. A loading dose of quinine was followed by others at 4- to 6-hour intervals in order to maintain a constant plasma concentration over a period of 4 to 8 days, which was checked by frequent drug estimations. After completion of the dosage schedule observation was started on the day after the final effective plasma level and was continued for 1 day in the event of disappearance of parasitaemia and fever. Remoculation with twice the original number of parasites was then carried out and observations were continued till parasites reappeared.

The therapeutic results were arranged in three classes as in the earlier experiments. In the 34 patients investigated, the results indicated that the therapeutic response to quinine was correlated with the duration of therapy (longer than in the experiments with *P. vivax*) and with the plasma quinine concentration. In similar experiments with another strain of *P. falciparum* (Costa strain) 21 patients were similarly investigated. The latter strain gives rise to a clinical picture like the other but the erythrocytic parasites from blood and sporozoite-induced infections nevertheless appeared to be more resistant to the suppressive action of quinine. The strains of *P. falciparum* employed showed greater resistance than the *P. vivax* strains to the suppressive action of this drug when judged in terms of plasma concentration. J. D. Fisher

TAGGART, J. V., EARLE, D. P. Jr., BERLINER, R. W., ZUBROD, C. G., WELCH, W. J., WISE, Nancy H., SCHROEDER, E. F., LONDON, I. M. & SUE, J. V. Studies on the Chemotherapy of the Human Malariae. III. The Physiological Disposition and Antimalarial Activity of the Cinchona Alkaloids. *J. Clin. Investigation*. 1943, May, 32: 74-83, 2, 60-63, (18 refs.)

Quinine has been the most widely used of the four chief cinchona alkaloids in the treatment of malaria, in spite of the fact that experiment has shown the others to possess comparable activity. On account of war needs further investigations were undertaken since supplies of cinchona bark containing the alkaloids other than quinine were readily available in the Western hemisphere. The present studies deal with the distribution, activity and toxicity of the four principal cinchona alkaloids in a quantitative manner with the aim of establishing a rational basis for their employment. The well known methods of BRODIE & UDENFRIEND this *Bulletin* 1943: 40-821, 1947: 44-793 were used for their estimation in biological fluids. The therapeutic tests and classification of results were similar to those employed in Parts I and II of this series (above). Particular attention was paid to the relationship between oral dosage and resulting plasma concentration. Absorption, distribution, degradation and excretion were also studied after oral administration in soft gelatin capsules over a period of 4 to 8 days.

It was found that the plasma concentration resulting from a particular dosage of any of the alkaloids varied widely in different individuals. The highest levels were attained with quinine and were lowest with cinchonine probably because the latter was largely metabolized rather than because of its deposition in tissues. Peak values were reached with a single dose by mouth within 3 hours, but persisted for short time only and soluble salts produced a higher

level than the alkaloidal bases. Maintenance doses of each, however, gave rise to the same equilibrium plasma concentration. Absorption from the gastrointestinal tract was almost complete as judged by the small amount of material excreted in faeces (less than 5 per cent), which consisted mostly of unchanged alkaloids. The concentration of quinine and cinchonine in plasma was more than 5 times that in the blood cells. In animals it has been shown [this *Bulletin*, 1944, v 41, 11, 1945, v 42, 778] that the concentration of these substances in organs and tissues is many times that in plasma. In man there appears to be little localization in tissues and no cumulative effect. Only a small percentage of the administered dose was excreted unchanged in the urine. The percentage of degradation products so excreted varied widely for the different alkaloids. Renal excretion plays only a minor part in regulating plasma concentrations of the parent substances, and in the body they undergo metabolic alteration to a large extent. One of the chief products formed in each case is the 2-hydroxyquinoline derivative, first isolated from quinine by KELSEY *et al* [this *Bulletin*, 1944, v 41, 923]. The derivative from cinchonine was shown to possess very little antimalarial activity. KNOX [this *Bulletin*, 1946, v 43, 1005] showed that an enzyme from rabbit liver could bring about a similar oxidation in all four alkaloids, but there is no evidence that the same enzyme is responsible for the oxidation in man.

The plasma concentration required to interrupt *P vivax* or *P falciparum* infections varied with each alkaloid, but the antimalarial activities of the four alkaloids did not differ widely. Cinchonine, however, showed a lesser activity against one strain of *P falciparum*. Cinchonism was encountered with quinine, and other unpleasant side-effects occurred with cinchonine, but only one patient showed idiosyncrasy to the former. It appears from the results obtained that any one of the four alkaloids is effective in control of clinical attacks of malaria provided that doses are given every 6 hours in order to maintain effective plasma drug levels. On account of their excretion and metabolism, these cinchona products are probably not so effective for suppression as some newer drugs with different distribution in the body.

J D Fulton

EARLE, D P Jr, WELCH, W J & SHANNON, J A. Studies on the Chemotherapy of the Human Malaria. IV The Metabolism of Cinchonine in relation to its Antimalarial Activity. *J Clin Investigation* 1948, May, v 27, No 3, Pt 2, 87-92 [12 refs]

The metabolic changes which a drug undergoes in the body may be of significance for the chemotherapeutic effect which it exerts. An investigation was undertaken from this viewpoint with cinchonine since it is known to undergo considerable metabolic changes in the animal body. KELSEY *et al* have carried out investigations in this field [this *Bulletin*, 1944, v 41, 11, 260, 1946, v 43, 404] while MEAD and KOEFLI [*ibid*, 1945, v 42, 9] showed that the substance obtained from quinine was the 2-hydroxy derivative. KNOX [this *Bulletin*, 1946, v 43, 1005] showed that there is an enzyme in rabbit liver which can oxidize the four chief cinchona alkaloids to a similar derivative. Most of the present data was obtained from normal patients. With the use of the method of FISHER *et al* (*J Pharm & Exper Therap*, 1943, v 79, 373) the amount of cinchonine and its 2-hydroxy derivative bound to albumin was found to be considerable. Absorption from the intestinal tract of the two substances was almost complete. From the urine, less than 5 per cent of the parent substance was recovered and more than 50 per cent of the 2-hydroxy derivative. The relationship between oral dosage and the blood plasma concentrations of each was determined by the well-known methods of BRODIE and UDENFRIEND.

[this *Bulletin* 1947 v 44 783] Results showed that when the parent substance or equal amounts of the two substances were given orally the resulting concentration of the derivative was greater in each case and its renal clearance was higher than that of cinchonine itself and was not depressed by doses of alkali to the extent that occurs with other organic bases. These differences were due largely to the greater rate of metabolism of cinchonine. The metabolite product was considerably less active than the parent substance against the McCoy strain of *P. vivax* when judged on the basis of plasma concentrations attained.

J. D. Fulton

TAGGART J. V. EARLE D. P. JR. BERLINER R. W. WELCH W. J. ZURBRUG C. G. JAILLIE J. W. KUTCH Beatrice H. NORWOOD J. & SHANNON J. A. Studies on the Chemotherapy of the Human Malaria. V. The Antimalarial Activity of Quinacrine. *J. Clin. Investigation*. 1948 May v 27 No. 3 Pt. 2, 93-7 1 fig.

As a result of the development of simple and accurate methods for the estimation of quinacrine (atebrin, mepracrine) by BRODIE and LINDSAY and by MASON [this *Bulletin* 1944 v 41 453 1945 v 42, 8] in biological materials and in various studies, including those of SHANNON *et al.* [ibid. 1945 v 42, 343] on its distribution in the body, the use of this drug in suppression and treatment of malaria was put on a rational basis. This report deals with the activity of the drug in terminating acute attacks of blood-induced *P. vivax* and *P. falciparum* malaria. The methods and strains employed were those described in earlier parts of this study. Suitable priming doses were given to obtain equilibrium plasma drug levels within a few hours, and the period over which drug was given was curtailed to prevent the continuance of significant drug levels in the blood beyond the desired 4 days in the case of *vivax* malaria and 8 days in the case of *falciparum* infections. The relationship between oral dosage, plasma concentrations and therapeutic effects are considered and indicate the range of effective plasma concentrations of the drug. The results obtained should be of value when the antimalarial activity of drugs of similar character is being studied. It is clear that the results depend to some extent on the species and strain of parasite used. The adequacy of dosage schedules in current use may readily be checked but details must be consulted in the original. J. D. Fulton

BERLINER, R. W. EARLE, D. P. JR. TAGGART J. V. ZURBRUG C. G. WELCH W. J. COXAN V. J. BAUMAN E. MUDDER S. T. & SHANNON J. A. Studies on the Chemotherapy of the Human Malaria. VI. The Physiological Disposition, Antimalarial Activity and Toxicity of Several Derivatives of 4-Aminoquinoline. *J. Clin. Investigation* 1948 May v 27 No. 3 Pt. 2, 98-107 1 fig. (20 refs.)

Russian workers before the late war appear to have regarded 4-aminoquinoline derivatives as of value in the treatment of malaria, but do not seem to have explored this group of substances to any extent. A number of derivatives, including S.N. 618 (Chloroquine) were synthesized in America during the war and certain members of the group appeared to show greater suppressive activity than quinacrine (mepracrine or atebrin) which they may be regarded as having some structural relationship if the latter were to suffer the loss of a benzene ring.

The present investigation deals with their physiological distribution, antimalarial activity and toxicity and included the study of absorption from the gastro-intestinal tract, renal excretion, distribution in tissues, combination with non-diffusible constituents of plasma as well as the relationship between

oral dosage and plasma concentration The methods of BRODIE, UDENFRIEND *et al* [this *Bulletin*, 1947, v 44, 793] were used for the drug estimations It was found that absorption of these substances was practically complete after oral dosage When equilibrium in plasma had been attained, 10 to 25 per cent of the daily dosage was accounted for by renal excretion, which was increased by the administration of acid and decreased by alkali as previously reported The unexcreted portion must suffer metabolic degradation All the drugs persisted in plasma for some time after the end of treatment The concentration of 4-aminoquinolines in the tissues of mammals was greater than in plasma There was some localization of the drugs in red and white blood cells As with quinine, these substances combined to a considerable extent with the non-diffusible elements of plasma

In testing antimalarial activity in blood-induced infections, the McCoy strain of *P vivax* and the McLendon strain of *P falciparum* were used, as described earlier The Chesson strain of *P vivax* was used for mosquito-induced infections The procedures were standardized and the results could be compared with those obtained with other drugs As a group, the 4-aminoquinolines showed high activity against both species of malaria The most active substances were derived from 7-chloro-4-aminoquinoline Administration of S N 7618 (Chloroquine) which is 7-chloro-4-(diethylamino-1-methylbutylamino)-quinoline in the dosage recommended [see this *Bulletin*, 1946, v 43, 708] over a period of one year showed that it was a safe suppressive agent, and S N 8137 (7-chloro-4-(3-diethylamino-2-hydroxypropylamino)-quinoline) showed similar characters and was of low toxicity J D Fulton

BERLINER R W EARLE, D P, Jr, TAGGART, J V, WELCH, W J, ZUBROD, C G, KNOWLTON, P, ATCHLEY, J A & SHANNON J A Studies on the Chemotherapy of the Human Malaras VII The Antimalarial Activity of Pamaquine *J Clin Investigation* 1948, May, v 27, No 3, Pt 2, 108-13 [16 refs]

Plasmoquine (pamaquin) was synthesized in Germany in 1926 by SCHULEMANN and his collaborators, and proved an active schizonticide in *P calhmanni* infections of canaries, but did not possess the same activity in human malaria Its most striking property was its activity against the gametocytes of *P falciparum* Its toxicity made it of limited value in treatment In combination with quinine it was believed to reduce the number of relapses in benign tertian infections SINTON [this *Bulletin*, 1930, v 27, 656] and JAMES, NICOL & SHUTE [*ibid*, 1931, v 28, 973] showed that it could act as a prophylactic in mosquito-transmitted malaria

The present authors have investigated the pharmacology and toxicity of pamaquin in order to get quantitative data on its suppressive activity in *P vivax* and *P falciparum* malaria and its curative action in sporozoite-induced *vivax* malaria, with a view to further development of this class of compound Dosage was arranged to produce uniform plasma concentrations over periods of 4 6 or 8 days, depending on the infection used, when the ability of the drug to suppress blood-induced infections was being studied The standard method of estimation [this *Bulletin*, 1947, v 44, 793] was employed The suppressive action was more marked against *vivax* than against *falciparum* infections, but strain differences were apparent, and in both the drug was relatively ineffective even at high dosage The low activity against the blood forms in *vivax* malaria made it difficult to determine whether the tissue phase of the parasite was affected At a dosage of 60/90 mgm daily in conjunction with 2 0 gm quinine over a period of 14 days it had a curative action in primary infections of





The following table records the maximum methaemoglobin values in patients who had received pamaquin for five or more days, by which time they attain a fairly stable level —

Treatment group	Number of subjects	Mean per cent methaemoglobin	Standard deviation	Range per cent methaemoglobin
pamaquin, 90 mgm daily	24	12.2	7.0	0.9-28.7
60        "	13	8.9	4.5	1.9-20.8
30        "	29	4.4	2.4	0.7-10.0
30        "	6	12.2	4.6	6.0-19.3
plus mepacrine				

The mean methaemoglobin values are proportional to the daily dose of pamaquin except for the small group that received quinacrine in addition here the values are equal to those recorded in subjects receiving a threefold larger dose of pamaquin. About half the patients in the first three groups were also receiving quinine, an addition that had no influence on methaemoglobin levels.

Acute haemolytic anaemia is the most serious hazard of pamaquin administration. It occurred in seven of 157 patients given pamaquin naphthoate in repeated doses for 2 to 14 days. Six cases occurred among 76 coloured patients, but only one among 81 white subjects.

The administration of 90 mgm of pamaquin a day for 14 days causes a significant reduction of mature neutrophile granulocytes. This reaction does not occur with daily doses of 30 mgm unless mepacrine is also administered. The process rapidly disappears when pamaquin administration is stopped.

Norman White

EARLE D P JR, BERLINER, R W, TAGGART, J V, ZUBROD, C G, WELCH, W J, BICELOW, F S, KENNEDY, T J JR & SHANNON, J A. *Studies on the Chemotherapy of the Human Malaria. X The Suppressive Antimalarial Effect of Paludrine*. *J Clin Investigation* 1948, May, v 27, No 3 Pt 2, 130-33 [13 refs]

The therapeutic trials described were carried out in patients with blood-induced malaria. The infections were the McCoy strain of *P. vivax* (28 patients), the Chesson strain of *P. vivax* which is more resistant than the McCoy strain to quinine, mepacrine and chloroquine (16 patients), and the relatively quinine-resistant Costa strain of *P. falciparum* (9 patients). Paludrine in varying doses, was administered by mouth. All doses are reported in terms of the free base. The therapeutic results are classified as follows: Class I, no certain effect, absence of parasitaemia for 14 days in McCoy strain or 21 days in Chesson strain or Costa *falciparum* infection, followed by a positive reinoculation. Paludrine was extremely effective against the McCoy strain of *P. vivax*. Total doses of paludrine as low as 50 mgm produced Class III results with regularity. It was only slightly less effective against the Chesson strain of *P. vivax*. The Costa strain of *P. falciparum* was much more resistant. Total doses of paludrine ranging from 338 to 750 mgm were given to the nine patients, Class III effects were obtained in only two.

The conclusion is reached that paludrine is the most active suppressive agent yet described in malaria, it is apparently non-toxic in therapeutic doses.

Norman White

BERLINER R. W., HENNEY T. J., Jr., & BIGLOW F. S. A Technique for the Detection of Minimal Numbers of Malaria Parasites Its Application in the Detection of Suppressed Virax Malaria. *J. Clin. Investigation* 1948, May 27 No. 3 Pt. 2 134-7

A technique is described for the detection of minimal numbers of *P. vivax* parasites in the circulating blood.

Fifty to 15 ml. of venous blood are drawn into a syringe containing sufficient heparin to prevent clotting. The blood is centrifuged for 20 minutes at 2,000 r.p.m. The plasma layer is carefully removed. The white cells are then aspirated off as completely as possible. The plasma is poured back and gently mixed with the red cells. The reconstituted blood is then carefully layered over an equal volume of bovine albumin solution in a centrifuge tube. (The albumin is prepared by diluting four parts of a 30 per cent. bovine albumin solution with one part of normal saline solution.) The tube is centrifuged for five minutes at 1,000 r.p.m. and then at 2,500 r.p.m. for 15 minutes. The material is now in three layers. The upper layer the plasma is discarded. The deepest layer consists of the normal red blood cells that have passed through the middle albumin layer. The latter contains the parasitized red cells which because of their diminished density and the viscosity of the albumin solution have been left behind. The albumin layer is removed and mixed with two or three volumes of isotonic saline in a centrifuge tube and centrifuged at 2,500 r.p.m. for five minutes. The red cells which have been driven to the bottom where they usually form a layer just sufficient to cover the bottom of the tube are transferred to a clean slide to form a thick smear which is dried and stained with Giemsa in the usual way.

With this technique the authors were able to confirm the observations made by FURLEY (this *Bullet.* 1945 4, 630) by subinoculation that the parasites of *P. vivax* first appear in the circulating blood 8½ days after the bite of infected mosquitoes and that the time of appearance is not influenced by suppressive drugs.

Attempts to concentrate parasites in *P. malariae* infections did not succeed. The parasitized cells are not enlarged. The same is true of cells containing young ring forms of *P. falciparum*.  
Norman White

ROSENFELD M., ZIMMOR C. G., BLAKE W. D. & SHANNON J. A. Methemalbumin. I. Appearance during Administration of Pamaquine and Quinine. *J. Clin. Invest.* 1948 May 27 No. 3, Pt. 2, 138-43 8 figs. (18 refs.)

A new compound of albumin and haematin which does not occur in normal serum, was described by FURLEY and BROWNE in cases of blackwater fever and later in cases of severe malaria, nocturnal haemoglobinuria, pernicious anaemia and other conditions, as well as after injection of large amounts of haemoglobin or of haematin. The compound was later named methemalbumin and its formation and properties described (this *Bullet.* 1945 32, 828; 1947 39, 270-271). It had also been observed by the authors in different conditions including pamaquine haemoglobinuria. The reaction between the two components was further investigated by KELLER (ibid. 1944 41, 1008). Its appearance was observed consistently by the present authors during combined pamaquine-quinine therapy but not when either drug was given alone.

Investigations were therefore carried out on four groups of male white volunteer malarial patients infected by mosquitoes with the Clonox strain of *P. vivax*. One group received pamaquine and quinine, a second group pamaquine

alone, a third quinine alone and a fourth pamaquin and quinacrine [atebrin, mepacrine]. Oral treatment was begun on the 5th day of fever, and two days later in the cases receiving pamaquin, being continued over a period of 14 days. Clear unhaemolysed serum was obtained before and after treatment from fasting patients, without the use of an anticoagulant, by centrifuging the blood for  $\frac{1}{2}$  hour when drawn. Methaemalbumin shows characteristic absorption and measurements were made in the Beckman spectrophotometer between 300m $\mu$  and 650 m $\mu$ , with diluted or undiluted serum according to the amount of pigment present. Chemical methods were also used for identification. The most intense absorption band occurs at 405m $\mu$  and was used for estimation in the absence of free haemoglobin. Allowance was made for absorption due to bilirubin which was estimated by chemical methods. Methaemalbumin was present in the serum of all patients of the group receiving combined pamaquin and quinine therapy, although in widely different amounts, and continued to increase during the period of treatment. Five days after therapy ended it was no longer present in measurable quantity, and was always absent from the serum of the other three groups. It was formed in the absence of frank haemolysis with which in the past it was most frequently associated. Methaemoglobin was also present in the red cells of patients receiving pamaquin alone or combined with quinacrine and quinine. The causal relationship between these two pigments, if any, is not clear.

J D Fulton

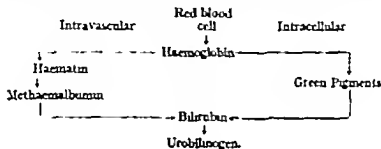
# BLAKE, W D Methemalbumin II Effect of Pamaquine and Quinine on Pathways of Hemoglobin Metabolism J Clin Investigation 1948, May, v 27, No 3, Pt 2, 144-50, 4 figs [21 refs]

It has been noted in Part I of this investigation [above] that methaemalbumin occurs during intravascular haemolysis and in a number of other conditions as well as after administration of pamaquin and quinine in combination. The regularity with which the pigment was produced by the two drugs together offered a means of studying its metabolism. The relationship of methaemalbumin production to haemolysis, the effect of drugs on its rate of disappearance as well as the part played by the liver, have been investigated in white patients with syphilis of the central nervous system. Some patients were investigated after malarial therapy when liver function had become normal. Pamaquin and quinine were given orally and their levels in plasma determined at regular intervals to ensure that absorption was taking place. Solutions of haematin and haemoglobin were given intravenously with few untoward results. Estimation of these two substances were made, and also of coproporphyrin, serum bilirubin and faecal urobilinogen.

The increase in amount of the faecal urobilinogen over controls was used as a measure of increased haemoglobin catabolism and occurred during combined therapy with pamaquin and quinine. When haemoglobin was given intravenously in an amount equal to the increased breakdown of this substance caused by combined therapy, no measurable formation of methaemalbumin occurred in normal subjects. It was concluded that haemolysis alone did not give rise to formation of this substance. Intravenous administration of haemoglobin in combination with oral quinine gave rise to the pigment, but when the three substances gave rise to the same degree of methaemalbuminaemia as pamaquin replaced quinine only traces of it were formed. A combination in combination of quinine with haemoglobin. It seems probable that the drugs haemoglobin broken down and also by interference in some way with the pathway of metabolism the first effect being a synergistic one and the latter due to quinine alone. It emerged that the rate of disappearance of haemoglobin

from serum was not affected by the drugs, but they did appear to slow down the rate of disappearance of the methaemalbumin formed. The effect of pamaquin in delaying conversion of methaemalbumin to bilirubin may be a result of interference with liver function, thus causing the former substance to accumulate on intra venous administration of haemoglobin. Quinine on the other hand, acts in some way by increasing the degradation of haemoglobin in the vessels to haematin.

Methaemalbumin is regarded as a normal product of haemoglobin metabolism whenever free haemoglobin is present in the serum. Severe haemolysis is necessary before methaemalbuminaemia becomes apparent, unless it is allowed to accumulate in serum as a result of its conversion to bilirubin being slowed down. The accompanying diagram indicates a possible metabolic pathway of intravascular haemoglobin.



J D Fulton

DE AZEVEDO J F CAMBOREXAC F J C. & PINTO M R. Observações sobre a incidência do zoonosismo na Guiné Portuguesa. (Nota preliminar) [Observations on the incidence of Malaria in Portuguese Guisasa—Preliminary Note.] *An. Inst. Med. Trop. Lisbon*. 1947 Dec. v 4 7 15 1 folding map. English summary

This note embodies the first results of an investigation initiated in Portuguese Guinea in January and February 1944 as part of the investigations launched by the Mission of the Tropical Medicine Institute of Lisbon. A total of 4 000 thick blood films were examined at first and eventually it was possible to deal with some 10 000.

Detailed regional findings are shown in a lengthy table and the incidence is shown graphically on a sketch map. *Plasmodium falciparum* was the common species, with *P. malariae* next; no *P. tertiarium* were found. Distribution of infection during the dry season was much more irregular than might be expected. There was no correlation between the percentage of persons infected with the particular species of parasite and the distance from the coast of the places where they were found.

H J O'D Burke-Gaffney

YOZELI M. Non-Pigmented Malaria Parasites in the Bone Marrow from a Mixed Infection of *Leishmania* and *Plasmodium* in a T. M. Roy Soc. Trop. Med. & Hyg. 1948, July v 42, No 1 93-100 1 pl

This paper records the finding in bone marrow smears of *Leishmania* parasites accompanied by malaria parasites resembling *Plasmodium* except for the important fact that the latter were devoid of pigment. The malaria parasites asexual and sexual, were all in red blood cells, but for the

absence of pigment, had normal morphology In examination of the peripheral blood before sternal puncture, no malaria parasites were found  
Without examination of the slides, no useful comment can be made  
H E Shortt

KETTLE, D S The Growth of *Anopheles sergenti* Theobald (Diptera, Culicidae), with special reference to the Growth of the Anal Papillae in varying Salinities *Ann Trop Med & Parasit* 1948, Apr, v 42, No 1, 5-29, 15 figs [26 refs]

This is a detailed study of the growth of the larva of *Anopheles sergenti* such of the paper is taken up with a statistical analysis of the recorded measurements, this part of the paper it is not possible to summarize, but in general, the object was to discover whether the anal papillae of larvae of anopheline mosquitoes grow during an instar and if so if their growth rate is the same as any other part of the body In preliminary experiments, second stage larvae of *A. multicolor* were used, when it was observed that the thorax grows in length and breadth throughout the instar but there is no sudden increase at ecdysis The head breadth remains more or less constant during the instar but shows a relatively enormous increase immediately after ecdysis The second abdominal segment and the dorsal anal papillae grow steadily in length throughout the whole of the larval life It is possible therefore to separate the different instars of *A. multicolor* on the head breadth But this species was rare and as *A. sergenti* was plentiful, the latter was used for this investigation

Five hundred larvae were used, 125 in each instar Seven measurements were made on each larva length and breadth of head, thorax and second abdominal segment and the length of the dorsal anal papillae The larvae in each instar were divided into six classes based on the size of the thorax breadth In diluted sea-water (equivalent to a 0.25 per cent solution of NaCl) the thorax and second abdominal segment grew steadily, the head grew hardly at all during each instar but increased enormously at each ecdysis, while the anal papillae lengthened during the instar and increased suddenly at ecdysis

The growth of the dorsal anal papillae was further investigated in larvae reared in various dilutions of sea-water The eggs from several females were mixed and then divided into eight batches which were reared under similar conditions other than the salinity of the water Fourth-stage larvae having a thorax breadth of  $1,000\mu$  were taken as standard, and of those kept in distilled water the papillae were very long ( $313\mu$ ), in tap water they were smaller ( $210\mu$ ) and in sea-water (equivalent to 0.1 per cent NaCl) they were  $190\mu$  There was no change as salinity increased to 0.75 per cent NaCl but in 1.0 per cent and 1.1 per cent they were distinctly shorter ( $152\mu$ )

The author discusses various suggestions which have been put forward to account for this variation in the lengths of the anal papillae of larvae reared in different salinities and concludes that while the enlargement in distilled water is regarded as a functional hypertrophy connected with the uptake of chloride ions, the nature of the mechanism which regulates the length of the papillae is unknown Whatever it may be, he suggests it is the same as that which controls the chloride content of the haemolymph  
H S Leeson

FAIN, A & HENRARD, C Quelques moustiques du fleuve Congo (Chenal) et des rivières Kasai et Kwango [Some Mosquitoes of the Congo, Kasai and Kwango Rivers] *Ann Soc Belge de Méd Trop* 1948, Mar 31, v 28, No 1, 7-20 [11 refs]

A list is given of the mosquitoes collected in African huts and European houses in villages along the Congo River from Léopoldville north to Kwamouth

east along the Kasai to Banningville and south along the Kwango for about 80 kilometres. Altogether nine anophelines and twenty six culicines are recorded. Generally speaking, in the riverine villages *Anopheles maculipes* was predominant, which may have been due to the time of collecting, after 7 p.m. Small numbers of *A. gambiae* were occasionally taken, but along the Kasai river *A. wellcomei* became so abundant that at Wusman Pool it outnumbered *A. maculipes*. *A. funestus* was taken once at one village in the interior where, however, *A. paludis* was the common species. *H. S. Lewis*

LEWIS, D. J. The Mosquitoes of the Jebel Auliya Reservoir on the White Nile. *Bull. Entom. Res.* 1948, May v. 38 Pt. 1 133-57 1 map, 6 figs. on 1 pl. & 3 text figs. (30 refs.)

The Jebel Auliya Reservoir is situated in the Sudan and extends some 530 kilometres up the White Nile from the dam of the same name. This area comprises the reservoir thousands of acres of seasonal swamps, irrigated areas and rain-water pools. The author discusses the topography, climate, population, vegetation, predaceous insects and fish and the effect of the dam on the breeding places of mosquitoes, of which forty-three forms have been found in the area.

Collections of mosquitoes were made during several visits to the reservoir between 1937 and 1948. Some results of collecting under various conditions in the Kawa section (the middle third) are summarized in four tables. Malaria occurs throughout the area and appears to have increased since the dam was constructed.

*Anopheles gambiae* is probably the main vector of malaria, and its breeding places which are comparatively small and well defined, can be treated with DDT in oil or with Paris green. *A. rufigipes* is provisionally regarded as a vector though of less importance than *A. gambiae*; its control would be a considerable problem as its breeding places are more extensive. Pyrethrum spray is used in houses against this species and parts of swamps are treated with Paris green dust or DDT in oil. *A. pharoscensis* is present in millions though of little importance as a malaria vector. The treatment against larvae is similar to that of *A. rufigipes*. *A. funestus* occurs in the south, in the Jelein section, though its northern limit is some miles further north in the Kawa section. Intensive house spraying appears to be the feasible method of control in the few villages that exist.

Paris green dust seems to be the ideal larvicide in this area because as it drifts with the wind its application does not necessitate wading in channels which may be infected with schistosome cercariae. An improved Paris green talcer is described and illustrated. *H. S. Lewis*

See also p. 1037. **ANNOTT** The Culexidae (Diptera) of Darfur Province, Anglo-Egyptian Sudan, with Observations on the Geography and Zoogeographical Relations of the Region.

MARR, L. The morphology of *Anopheles gambiae* (Diptera: Culicidae). *Bull. Entom. Res.* 1948, May v. 38 Pt. 1 133-57 1 map, 6 figs. on 1 pl. & 3 text figs. (30 refs.) *L. S. Lewis*

ROBERTS, F. H. & O'SULLIVAN, J. J. Studies on the Behaviour of Adult Australasian Anophelinae. *Bull. Entom. Res.* 1948, May v. 38 Pt. 1 159-74 graph & 1 fig. 10 figs.

Observations were made on adult anopheline mosquitoes at Cairns, North Queensland from January to April 1944 and at Salamaua, New Guinea from

May to July, and at Mirivasi, New Guinea from August to October. The species studied were *Anopheles punctulatus*, *A. p. farauti* and intermediate forms, and *A. amictus hilli*. The authors record in detail their investigations into prevalence and activity, by day and by night, biting habits, daytime haunts, host preferences and methods of determination of the age of female mosquitoes by condition of the wings, ovarian development and state of digestion.

All forms of *A. punctulatus* have much in common, though behaviour may differ slightly according to local conditions. Adults usually disperse from breeding places and congregate around the source of the blood meal, for example, human settlements. Greatest activity commences after dark but no marked periodicity was observed at dawn and dusk, as has been widely held. They do not indulge in long continuous flights but females have been found a mile from breeding places and males 600 yards away. After feeding, the females rest in the huts a short time, then fly out, their outdoor resting places are among vegetation near the ground, other females and males also are there and fertilization is assumed to take place here, not at the breeding place, males do not normally enter houses but stay in the bush. Pyrethrum sprays in huts in the daytime have therefore little effect, but the application of DDT to the walls is more promising. Precipitin tests showed that *A. p. farauti* has no pronounced preference for either animal or human blood but in *A. p. punctulatus* anthropophilism was marked. All forms seemed more attracted to the indigenous people in Salamaua than to the white man.

The behaviour of *A. amictus hilli* is similar in most respects to that of the *punctulatus* forms. One difference was, however, noted. *A. a. hilli* gathers in large numbers around the breeding places, where the males remain, and fertilization probably takes place here and not in the bush. The daytime resting places of females awaiting a meal were not determined and the host preferences were not fully explored by the precipitin test, but this anopheline is known to be a vicious pest in Northern Queensland.

Very little is known of the habits of other anophelines. *A. bancrofti bancrofti* rarely attacks man at Cairns, but in the Northern Territory has been reported to have an infection rate of 4.3 per cent. *A. annulipes* is an extremely common species, well distributed throughout Australia and extending into New Guinea. It is probably a malaria vector in sporadic cases outside the *farauti* area. [See also this *Bulletin* 1945, v 42, 1049, 1947, v 44, 275.] H S Leeson

ROZEBOOM L. Transmisión de la malaria en el Nuevo Mundo [Transmission of Malaria in the New World] *Medicina* Mexico 1948, Feb 25 & Mar 10 v 28 Nos 550 & 551 85-93 100-112

BASHAM Ernestine H. & HÆGER J S. Records of *Anopheles quadrimaculatus* Say for the Florida Keys. *Mosquito News* 1948 June v 8 No 2, 72

PEFFLY R L, DAVIDSON R H & WATERS, H A. Studies in Laboratory Rearing of *Anopheles quadrimaculatus* Say. *Ohio J Sci* 1946 v 46, No 2 65-70 2 figs

GOUTINHO J DE O. Contribuição para o estudo da distribuição geográfica dos anofelinos do Brasil. Sua importância na transmissão da malária [Geographical Study of Anophelines in Brazil and their Importance in Transmission of Malaria] [Thesis] Universidade de São Paulo, Faculdade de Medicina 1947, Dec, 117 pp, 2 maps [Bibliography]

According to the present author there are in Brazil 48 species of *Anopheles* and 3 of the related genus *Chagasia*. A table gives the distribution of the *Anopheles* in the separate states of Brazil

The bulk of the paper takes separate states and in each shows the local distribution of the species of *Phlebotomus* which occur, the proportion of adults found in houses and so forth. The thesis contains a wealth of local detail.

In Brazil, *Plasmodium* has been found in six species of *Phlebotomus*. The salivary gland rate was 1.53 per cent. of 579 *P. darlingi*; the rate was between 0.35 and 0.20 per cent. in considerable numbers of *P. larumaculatus crumii*, *lellator* and *homunculus*. It was 0.07 per cent. in 3,938 *P. albimanus*.

P. J. Dutton

LAMPEN H. Induzierte Malaria nach Bluttransfusion. [Malaria transmitted by Blood Transfusion.] *Med. Klin.* 1947 May, v. 42, No. 9, 371-2.

Owing to the risk of disease being transmitted by blood transfusion a law was passed in Germany in March, 1940 that donor must be free from tuberculous, skin disease, venereal or tropical diseases. In spite of every care this freedom from infection cannot always be guaranteed. The author quotes the case of a man who in May 1943 was given a transfusion of 450 cc. of blood on account of anaemia produced by peptic ulcer. Great pains had been taken to eliminate risk of the diseases mentioned, but just a month later on the 7th, 9th, 12th and 14th days of June, the patient had attacks of fever and shivering, and examination revealed tertian malaria parasites in his blood. The donor had not had a day's illness for more than 20 years, but a history was obtained (although no parasites could be seen in two examinations of his blood) that in 1915 or 23 years before, he had been a prisoner of war in Southern Russia and had there suffered from malaria, tertian type, but though he had occasional attacks for 5 years afterwards, he had been quite free from them since 1920 that is 23 years before his blood was used for transfusion. All other sources seemed to be excluded.

H. Harold Scott

ARO L. La ricerca del parassita malarico mediante arricchimento. (Nota di tecnica.) [Kartekman's Method for finding Malaria Parasites.] *Riv. di Malariologia* 1948, Feb., v. 27, No. 1, 47-50, 3 figs. English summary.

After brief reference to methods of detection of malaria parasites, by special staining, by thick drop and enrichment methods, the author describes the one used at the Institute of Hygiene and Bacteriology of the University of Cagliari and Sardinia. Five cc. of blood are taken from a vein into citrate and centrifuged at a low speed for 15 minutes with a capillary pipette are drawn off, first the serum (? plasma), then the layer of leucocytes and the platelets which lie above the red corpuscles. Care is needed because if many white cells are left the resulting preparation is confused. The parasites are fixed by 10 per cent. formal for 20 minutes and the red cells haemolysed in 20-30 cc. of 0.35 per cent. NaCl for 10-15 minutes. The whole is then centrifuged for 5 minutes, the supernatant fluid is removed leaving two or three drops for emulsifying the deposit. Preparations are spread from this dried in the thermostat or at room temperature and stained with Giemsa's stain, 10 per cent. The author claims that this procedure gives permanent preparation and a concentration of 50-150 times the original.

H. Harold Scott

V. HALLER E. Über die Ursache und das Auftreten von Rückfällen bei der Malaria tertiana. [An Examination of the Origin of Relapses in Tertian Malaria.] *Med. Klin.* 1947 May, v. 42, No. 10, 41-17 charts.

The essence of this paper is to be found in the theoretical considerations which have convinced the author that in benign tertian malaria an infection cycle which he presumes to be in the endothelial cell of the capillaries, must take



The reasoning which has led him to these conclusions is now well understood, but he is, of course, ignorant of the recent classical demonstrations by SHORTT and GARNHAM. A detailed review of this communication has now lost its chief point, though it is interesting to observe how near to the real truth his arguments are. He observes, for instance, how in the Sardinia-infected military cases relapses of *P vivax* were extremely uncommon, whilst in a prisoner-of-war hospital on the Adriatic coast nearby they were invariably the rule. This anomaly he would explain by the disparity in the primary dose of sporozoites. On the persistence of the EE cycle the spring and autumn relapse of primary infections can also best be explained. He asserts too that the timing of relapses is due to the presence or absence of immune bodies in the blood stream, which destroy the merozoites on liberation from the tissue stages—another prophecy which bids fair to come true, and he suggests that these immune substances can exert no action on the EE forms. In this respect the reaction is the same whether the primary infection is slight or severe. Any therapeutic measures which are directed towards the extirpation of the erythrocytic stages cannot prevent relapses from occurring at their predestined intervals, so that the only reasonable therapy is one directed towards the destruction of the tissue stages of the parasite. The absence of any provocative factors cannot be regarded as of any prognostic significance.

All these arguments now resound with a genuine ring P Manson-Bahr

LOMBARD Frances F *Review of Literature on Cinchona Diseases, Injuries, and Fungi* U S Dept of Agric *Bibliographical Bull* No 9 Wash. 1947, Dec, 70 pp [290 refs] Superintendent of Documents, U S Govt Printing Office [20 cents]

WINCKEL C W F *De vermindering der recidieven van malaria-aanvallen door behandeling met kinine en plasmoquine* [The Reduction of Malarial Relapses with Quinine and Plasmoquine] *Nederl Tijdschr v Geneesk* 1948, Aug 14, v 92 (iii) No 33 2507-16 [Refs in footnotes]

A general review

MAIER, J *The Absorption of Quinine and Quinacrine in Dysentery Patients.* *Amer J Trop Med* 1948, May, v 28, No 3, 397-400

During the recent war American troops in New Guinea frequently suffered from malaria and dysentery at the same time, in spite of the fact that quinacrine (mepacrine) in 0.1 gm. daily doses was supposed to be taken as a routine. It seemed possible that in these circumstances the drug was not being absorbed. Investigations were therefore carried out on patients with severe or moderately severe dysentery to determine whether oral quinacrine or quinine was normally absorbed or whether some other form of administration was necessary. The patients were divided into three groups and received treatment according to the following dosage schedules. Group I, consisting of 14 patients, were given 40 grains of quinine daily as well as intensive sulphaguanidine treatment, non-dysentery patients were used as controls and received the same drug treatment. A similar number of patients in Group II received intensive sulphaguanidine treatment along with 3 doses of 0.3 gm. quinacrine on the first day and 3 of 0.2 on the second day. Plasma levels of both drugs were determined by the method of BRODIE & UDE-FRIEND [this *Bulletin*, 1944, v 41, 453]. The 19 patients in Group III were given 3 doses of 0.3 gm. quinacrine only on the day of admission and the plasma drug level was measured. Quinacrine plasma

levels were also measured in two patients without dysentery but who were also receiving sulphaguanidine. This substance did not interfere with quinacrine estimations.

There was no relationship between the severity of diarrhoea and the plasma levels of the drugs. It was concluded that the drugs were absorbed in the normal way when given by mouth to patients with diarrhoea as the result of acute bacillary or non-specific infection.

J. D. Fulton

KARLSTORF. A. Ueber eine Leberschädigung durch hohe Atlebrindosen.  
[Damage to the Liver from Large Doses of Atlebrin.] *Altn. Woch.* 1947  
July 15 v. 24/25 Nos. 39-40 637-3.

Considering how widespread has been the use of atlebrin (mepacrine) in malarial conditions, reports of untoward by-effects have been surprisingly few. Except for gastro-intestinal disturbances on the whole mild in degree, the chief have been mental or psychic—a sense of fatigue and depression leading perhaps to thoughts of suicide.

In the present contribution the author records the case of a young soldier 21 years of age hitherto enjoying the best of health. He gave a history of having taken in 3 weeks 6 small tablets of atlebrin and in the following week 10 " large tablets—at least 5 gm. altogether (probably more). He became jaundiced and was admitted to hospital. The upper part of the abdomen was tender to pressure but the liver was not at that time enlarged. During the ensuing fortnight the jaundice increased. The urine gave a strongly positive acridine reaction, the Takata-Ura reaction of the serum was marked and the liver was enlarged and could now be felt three fingers breadth below the costal margin. There was increased excretion of galactose in the urine after 50 gm. were taken—in successive hours 1 gm., 1.23 gm. and 0.5 gm., or " 43 gm. altogether.

The hepatic condition it was concluded, was due to the atlebrin taken. Further investigations are to be undertaken to determine the pathogenesis of the action of the drug, and whether the damage to the parenchyma is due to its action on the liver capillaries.

H. Harld Smith

WALLS E. S. Paludrine. Correspondence. *Brit Med J.* 1948, July 4  
225-d.

Walls writes from Sierra Leone. He has not found that paludrine in doses of 0.1 gm. twice a week can be relied upon to prevent attacks of malaria in himself or his patients, but in doses of 0.1 gm. each day it is about equal to quinine and mepacrine in its suppressive effect and has the advantage that it is not toxic and does not stain the skin. For treatment he gives 0.1 gm. three times each day for 10 days and on the first day he also gives two doses of quinine (10 grains each).

In general, he prefers paludrine to the other drugs, but in doses greater than those hitherto recommended by the maker.

Charles Wallis

ROBERTSON J. D. Paludrine Treatment of School Children. *Zentralbl. Bakt.* 1948, April 11 45.  
& *Suppl. 93* v. 134 December 1947.

This interesting work reported by Dr. J. D. Robertson of the Zanzibar Hospital, about 50 children in each of three schools of mainly African population, given 0.1 gm. paludrine twice daily each week from September 1947. In addition the children in the school were given and followed on the remaining days. A fourth group of pupils from one of the schools received no paludrine or

other medication and served as a control The children were examined for spleen and parasite rates before treatment and again in 6 weeks and 3 months The parasite rate, which averaged 50 per cent initially, fell to nil in the treated children in 6 weeks, and although it "tended to fall naturally" the controls still showed a rate of 26.8 per cent after 3 months Splenic enlargement fell from 60 per cent to 18 per cent over the period of treatment, but remained at 56 per cent in the untreated controls The haemoglobin levels were unchanged in all groups and the iron supplement caused no improvement

The figures for the rates in each group are shown in three tables the author concludes that the dosage of paludrine, 0.1 gm twice weekly, was a little too small to be completely effective  
H J O'D Burke-Gaffney

ANSARI, M Y **Anti-Malarial Drugs Old and New, with some Observations on Paludrine in Malaria** *Indian Physician* 1948, July, v 7, No 7, 177-84

This paper is largely a review of the relative efficacy of the different anti-malarial drugs, but it contains a personal observation by the author on the use of paludrine in the treatment of about 20 patients suffering from benign tertian and malignant malaria [further details of the cases are not given]

The drug was used in dosages ranging from 50 mgm to 300 mgm daily, and was administered as (1) a single initial dose of 300 mgm and then 100 mgm twice daily for 14 days, (2) twice daily doses of 100 mgm for 14 days, (3) 25 mgm as effective as (2) above

It is stated that "with the dosage mentioned above and the method used", temperatures became normal in 1 to 3 days and parasitaemia disappeared in 2 to 4 days There were no relapses during the patients' stay in hospital (7 to 35 days) No toxic effects were noted with these dosages Gametocytes were unaffected  
H J O'D Burke-Gaffney

MAEGRAITH B G **Paludrine in the Treatment and Control of Malaria** *An Inst Med Trop* Lisbon 1947 Dec v 4 413-26 2 folding figs [14 refs]

A lecture given at the Institute of Tropical Medicine, Lisbon

FITZHUGH O G NELSON, A A & HOLLAND, Oma L **The Chronic Oral Toxicity of Chloroquine** *J Pharm & Exper Therap* 1948, June, v 93, No 2 147-52 1 chart

Chloroquine (SN 7618), which is 7-chloro-4-(4-diethylamino-1-methylbutyl-amino) quinoline, was synthesized during the last war in America and proved an active antimalarial agent A report on its properties was made by LOEB [this *Bulletin* 1946 v 43, 708] and WISELOGLE [Survey of Anti-malarial Drugs 1941-1945, *ibid*, 1947, v 44, 1106] According to Most *et al* [*ibid*, 1946, v 43, 1011] it appeared to be more active than quinine and quinacrine (atebrin mepacrine) in *P vivax* infections under the conditions of test The present report in which experiments lasted 2 years compares the earlier results of the authors [*ibid*, 1946, v 43, 525] on the chronic oral toxicity of quinacrine with those obtained with the newer drug

Groups of 10 male and 10 female rats 21 days old were given six diets containing from 100 to 1000 ppm chloroquine, to which they had free access in individual cages under controlled conditions of temperature and humidity

The growth of rats on the diet with 100 and 200 p.p.m. did not differ from controls. With 400 p.p.m. there was early retardation of growth, but at the end of one year the variation from controls was not significant. Higher doses reduced growth and caused death within a year. Leucocytosis, chiefly neutrophilic, resulted from continued administration of medium or high doses. Haemoglobin and red cell numbers were also increased by the latter.

The principal lesions encountered were a focal necrosis of striated muscle especially cardiac and necrosis and fibrosis of the central lobules of the liver. There was a marked distinction in frequency and severity of the lesions between 400 and 800 p.p.m. dose levels. At 200 p.p.m. or below lesions were slight. From calculation it appeared that the dosage of chloroquine which would produce toxic effects in rats is higher than either the therapeutic or prophylactic dosage recommended for man. The general inference of the authors was that chloroquine is slightly less toxic than quinine for rats. The pathological lesions caused by these drugs showed similarities.

J. D. Fulton

STRAUS, B. & GEXXIS, J. Evaluation of Pentaquine as a Cure of Relapsing Vivax Malaria. A Controlled Study of Ninety Five Cases. *Bull. New York Acad. Med.* 1948, June & 24 No. 6, 393-6.

This study was designed to test the efficacy of pentaquine combined with quinine in the therapy of naturally acquired *P. vivax* infections in man. The patients were servicemen in the Veteran Administration Hospital, Bronx, New York and totalled 83. 84 of them had served in the south-west Pacific theatre. All had *P. vivax* infections. Controls were made with chloroquine (5N 7618) because it is highly effective in treatment of the attack but has little if any effect on relapses. It was given as the diphosphate in a dosage of 0.6 gm. of base followed in six hours by 0.3 gm. and 0.3 gm. on the 2nd and 3rd days. Pentaquine was given as the monophosphate in a daily dose of 30 mgm. base (10 mgm. every 8 hours) with 0.4 gm. of quinine sulphate for 14 days. The dosage of pentaquine is half the recommended daily dose of 60 mgm. of base. This reduced dose was used to decrease toxicity and was regarded as feasible as it was likely that most of the men would have had some degree of immunity.

The study began in January 1947 with 48 patients in the chloroquine group and 49 in the pentaquine-quinine group. Follow up, which varies from 1 week to 14 months, will continue for at least a year. At present 83 per cent. of patients have been followed up for more than 4 months. To date none of the patients in the pentaquine group have relapsed. 14 of the chloroquine group have relapsed (12 from the S.W. Pacific). One patient had three relapses and two had two relapses.

Toxic manifestations in the pentaquine-quinine group were mostly insignificant though some did occur in 75 per cent. of patients. In no case was it necessary to discontinue pentaquine though quinine had to be discontinued in one case. Nausea, anorexia and occasionally vomiting, occurred commonly in the first 4 days and mild abdominal pain after the first week. Tinnitus, diarrhoea and headache were not uncommon. Six patients showed a decrease of 1 million red blood cells or less per cmm. but no frank haemolytic reactions were seen. Fever (99.6°-100.4 F) lasting for one day occurred in 7 patients from the 7th to the 11th day. It is suggested that many of the toxic manifestations were probably due to quinine.

The results so far suggest that one-half of the previously recommended dosage of pentaquine eradicates relapsing *vivax* malaria.

H. J. U'D. Burleson/Hyney

WRIGHT C I & SABINE, Jean C, with technical assistance of Anne H WRIGHT  
**Cholinesterases of Human Erythrocytes and Plasma and their Inhibition  
 by Antimalarial Drugs** *J Pharm & Exper Therap* 1948, June, v 93,  
 No 2, 230-39, 5 figs [20 refs]

The study now reported forms part of a wider investigation undertaken to find if any relationship exists between antimalarial activity and toxicity of chemical compounds and their inhibitory action on cholinesterase. The enzyme present in red cells and plasma was used, as qualitative differences have been ascribed to them. The antimalarial drugs employed were quinine, quinidine, plasmoquine, quinaquine [atebrin, mepacrine], chloroquine and paludrine. Their inhibitory power was estimated manometrically by their effect on hydrolysis of acetylcholine. Suitable dilutions of the enzyme preparations were in the reaction flask and acetylcholine was added from the sidearm. Chloroquine and quinaquine inhibited the enzymes from both sources about equally, while the remaining four drugs were less effective against that from red cells. There was no correlation between inhibitory action on cholinesterase and antimalarial activity or toxicity. *J D Fulton*

MACDONALD G **The Policy of Malaria Prevention** *An Inst Med Trop* Lisbon  
 1947 Dec, v 4 373-90 [12 refs]  
 A lecture given at the Institute of Tropical Medicine, Lisbon

MACDONALD G **The Place of DDT as an Anopheline Larvicide** *An Inst Med Trop* Lisbon  
 1947 Dec, v 4 391-411 5 figs (2 on 1 pl) [18 refs]  
 A lecture given at the Institute of Tropical Medicine, Lisbon

WATERHOUSE, D F, ATHERTON, D O **Spray Tests against Adult Mosquitoes**  
**1 Laboratory Spray Tests with Culex (Culex fatigans) Adults** [WATERHOUSE] *Commonwealth of Australia Council for Sci & Indust Res Bull*  
 No 219, pp 1-27, 3 figs [11 refs] **2 Spray Tests with Anopheline (Anopheles punctulatus farauti) Adults** [WATERHOUSE & ATHERTON] *Ibid*,  
 pp 29-40, 2 pls

1 The first paper deals with initial exploratory tests of sprays against *Culex fatigans* under standardized laboratory conditions in Canberra, during 1942 and 1943. They were designed to provide information on the minimum effective concentration of pyrethrins and also to evaluate the effectiveness of Lethane, Thanite, DDT and other synthetic materials.

Eggs of *C fatigans* were collected in the field and reared to adult stage in the laboratory at  $80 \pm 1^\circ\text{F}$  ( $26$  to  $27^\circ\text{C}$ ) and  $70 \pm 2$  per cent relative humidity. The adults were kept in cages for four to six days after emergence and fed on fruit, not blood. The tests were made in a Peet-Grady chamber with the standard spray gun and a 2 ml dosage (one-sixth of the standard dose for flies) equivalent to 1 fl oz per 3,000 cu ft. The spray was applied at 12.5 lb air pressure and the mosquitoes remained exposed to the mist for ten minutes. They were then all collected and after the percentage knockdown was calculated, were transferred to a clean cage with fresh apple and left for twenty-four hours.

About 350 tests were made on more than 30,000 mosquitoes. The results show that a spray of 0.14 per cent pyrethrins gave 99.3 per cent knockdown and kill. DDT and Thanite also showed promise. A spray containing 1.0 per cent DDT gave 94 per cent mortality but only 55 per cent knockdown, the addition of 0.1 per cent DDT to a 0.01 per cent pyrethrins spray increased mortality by 16 per cent. A 3.5 per cent Thanite spray was about equal in

effectiveness to the 0.14 per cent. pyrethrins spray but 0.5 per cent. Thanite added to a 0.01 per cent. pyrethrins spray resulted in a lowering of both knockdown and mortality. Lethane was neither highly toxic to the mosquitoes nor did it serve any useful purpose when added to a pyrethrum spray. Other synergists had little or no effect on pyrethrum sprays used against *C. fatigans*.

2. The second series of tests was an extension of the laboratory experiment recorded in the first paper. They were made in tents or native huts with caged wild-caught females of *Anopheles punctulatus farauti* at Lalapeli in New Guinea in September 1943. Dosages of 1 fl. oz. per 2,100 cu. ft. and 1 fl. oz. per 3,000 cu. ft. were atomized by pressure sprayer and by hand spray gun. An interval of ten minutes was allowed and the percentage knockdown noted. The tent was aired for twenty minutes and mortality rates were recorded after 1.5 and 18-20 hours. Temperature varied between 82 and 90 F. (27.5 and 32° C.) and relative humidity between 68 and 82 per cent. A total of 10,800 female mosquitoes were used in 238 experiments in which 32 sprays were tested.

The results agree (except for Thanite sprays) with the laboratory tests on *C. fatigans* described in the first paper. The reason was probably the greater fumigating effect in the Pett-Grady chamber.

For sprays containing pyrethrins alone it would not be desirable to use solutions weaker than 0.07 per cent. pyrethrins which gave 88.5 per cent. knockdown and 89 per cent. kill (concentrations above this gave complete kill and knockdown). A 0.5 per cent. DDT spray gave 97 per cent. mortality but only 33 per cent. knockdown. However the addition of 0.03 per cent. pyrethrins improved the knockdown to 68 per cent. Five per cent. Thanite did not give sufficiently high kill, but a 3.5 per cent. Thanite-0.5 per cent. DDT mixture gave good knockdown and high mortality. The use of such an unpleasant spray would only be justified if pyrethrins were not available.

In practice these sprays gave freedom from attack by *A. farauti* for about 6-8 minutes and they had no persistent lethal effect but the application in use tent, of DDT at the rate of 50 mgm. per sq. ft. freed it of resting anophelines for some weeks.

The evidence provided by the tests in the second paper confirmed the decision of the Australian Army authorities not to vary the 0.14 per cent. pyrethrins spray adopted provisionally as a result of the test reported in the first paper and not to include a synergist. This was used until the advent of DDT in the last year of the war in sufficient quantity to reinforce the spray and convert it into an all-purpose one.

H. S. Leach

**BRITISH GUIANA.** Report of the Honorary Government Malariaologist for the Year 1947. GIGLIOTTI, G. Mosquito Control Operations by Residual D.D.T. in British Guiana. Filariasis Survey of the Coastlands. 14 mimeographed pp. 1 map.

In January 1947 the Yellow Fever Service and the Malaria Research Unit of British Guiana were combined into a Mosquito Control Service. The DDT residual spraying of houses was made compulsory in localities declared DDT control areas by the Director of Medical Supplies.

Meteorological and population figures are listed and the organization of the spraying unit is described. Malaria is either endemic or sub-pendemic in the coastlands exterior and in parts and peripheries of towns. In the interior it is widely and by endemic in most communities. The vector is *Anopheles farauti* in the coastlands and *A. tritaeniorhynchus* in the interior. *A. farauti* is not a true vector but it is a very important transmitter of malaria but they are not true vectors and possibly maintain small foci of malaria in the north-west where *A. tritaeniorhynchus* is present. These foci are not true foci but are maintained by DDT house spraying.

The aim is to treat all buildings in control areas with 150 mgm DDT per square foot at intervals of eight months, which may later be extended to 10 or even 12 months. In 1947, 32,458 buildings in the coastal area were treated, involving 262,832 persons or 89 per cent of the coastal population and 70 per cent of the total population. Spraying in the remaining parts is now proceeding. In the interior, considerable spraying was done by the mining companies.

Immediately after treatment, adults of *A. darlingi* disappear and larvae disappear two or three weeks later. It is claimed that in these areas *A. darlingi* has now been eradicated. Figures are given to show the reduction in spleen rates and the slower reduction in the parasite rates.

A survey of filariasis is proceeding and figures are given for 1946-47 showing the distribution by race, sex and age and the degree of infestation, etc. It is expected that the effect of the DDT sprayings on the incidence of filariasis will be much slower in its development than it is on the incidence of malaria.

A monograph on mosquito-borne diseases in British Guiana and on three years of investigation on their control by DDT is being prepared and will soon be available.

The report concludes with a list of publications issued during the year  
H S Leeson

PRATT, H D **Relation of Plants to Malaria Control in Puerto Rico** *Supplement No 200 to Pub Health Rep* Wash 1947, Dec, 38 pp, 3 charts & 10 figs [11 refs]

This paper describes plant communities in Porto Rico and their relations to anopheline production. Various plant associations are described and control methods appropriate to them.

Examples are, the control of *A. albimanus*, breeding in mangrove swamps by drainage, dusting and "salting up" from sea-level canals, and the drainage of flats and oiling of temporary pools where *Batis maritima* and *Sesuvium portu-lacastrum* dominate and lead to the breeding of *Aedes taeniorhynchus*, *Aedes sollicitans* and *Psorophora confinnis* and *P. pygmaea*. In coastal swamps where *Typha angustifolia* and *Phragmites* dominate, *albimanus* breeds only at the sunlit margins, and drainage and dusting with Paris green has been successful. For grasslands and pasture, where temporary pools in small depressions or in hoofmarks may lead to heavy breeding the plant associations are dealt with in some detail. It is pointed out that tall grasses may render larvicidal methods difficult and control by drainage is recommended. Sugar-cane fields present a special problem. In newly cut fields there is little breeding, but as the trash sinks into the irrigation ditches and the water surface becomes sunlit, and especially when the ditches are reflooded after fresh planting, then *A. albimanus* increases until after the canes reach a metre in height, when *A. grabhamus* gradually replaces *albimanus*. When the canes are at full height, *A. vestitipennis* may be the only species present.

Plants which tend to inhibit anopheles production are listed, such as duckweed, *Azolla*, *Pistia* and other species which make floating mats. *Ceratophyllum demersum*, on the other hand, produces mats beneath the surface and so protects anopheles larvae from natural enemies, and, in Porto Rico this species is particularly associated with *albimanus*. Other plants of similar habit (*Chara Utricularia*) have the same effect.

The use of the cable saw for clearing subaquatic vegetation, plants useful in bank sodding and the methods used for eliminating *albimanus* breeding in flotage in sheltered water behind sandbars are also described. Finally, a key, based on simple vegetation characteristics, to the 138 important plant species associated with anopheles in Porto Rico is given.  
C G Johnson

effectiveness to the 0.14 per cent. pyrethrins spray but 2.5 per cent. Thanite added to a 0.01 per cent. pyrethrins spray resulted in a lowering of both knock down and mortality. Lethane was neither highly toxic to the mosquitoes nor did it serve any useful purpose when added to a pyrethrum spray. Other synergists had little or no effect on pyrethrum sprays used against *C. fatigans*.

2. The second series of tests was an extension of the laboratory experiments recorded in the first paper. They were made in tents or native huts with caged wild-caught females of *Anopheles punctulatus* fed at Lalapagi in New Guinea in September 1943. Doses of 1 fl. oz. per 2,100 cu. ft. and 1 fl. oz. per 3,000 cu. ft. were atomized by pressure sprayer and by hand spray gun. An exposure of ten minutes was allowed and the percentage knockdown noted. The tent was aired for twenty minutes and mortality rates were recorded after 1.5 and 18-20 hours. Temperature varied between 82 and 90 F. (27.5 and 33° C.) and relative humidity between 68 and 92 per cent. A total of 10 dead female mosquitoes were used in 238 experiments in which 32 sprays were tested.

The results agree (except for Thanite sprays) with the laboratory tests on *C. fatigans* described in the first paper. The reason was probably the greater fumigating effect in the Pet-Grady chamber.

For sprays containing pyrethrins alone it would not be desirable to use solutions weaker than 0.07 per cent. pyrethrins which gave 99.5 per cent. knockdown and 99 per cent. kill (concentrations above this gave complete kill and knockdown). A 0.5 per cent. DDT spray gave 97 per cent. mortality but only 33 per cent. knockdown; however the addition of 0.01 per cent. pyrethrins improved the knockdown to 98 per cent. Five per cent. Thanite did not give sufficiently high kill but a 3.5 per cent. Thanite + 0.5 per cent. DDT mixture gave good knockdown and high mortality. The use of such an unpleasant spray would only be justified if pyrethrins were not available.

In practice these sprays gave freedom from attack by *A. p. fatigans* for about five minutes and they had no persistent lethal effect but the application in one tent of DDT at the rate of 50 mgm. per sq. ft. freed it of resting mosquitoes for some weeks.

The evidence provided by the tests in the second paper confirmed the decision of the Australian Army authorities not to vary the 0.14 per cent. pyrethrins spray adopted provisionally as a result of the tests reported in the previous paper and not to include synergist. This was used until the advent of DDT in the last year of the war in sufficient quantity to reinforce the spray and convert it into an all purpose one.

H. S. LECHE

BRITISH GUIANA. Report of the Honorary Government Malariaologist for the Year 1947 (GIGLIOLI G. Mosquito Control Operations by Residual D.D.T. in British Guiana. Filariasis Survey of the Coastlands. 14 mimeographed pp. 1 map.

In January 1947 the Yellow Fever Service and the Malaria Research Unit of British Guiana were combined into Mosquito Control Service. The DDT residual spraying of houses was made compulsory in localities declared DDT control areas by the Director of Medical Supplies.

Meteorological and population figures are listed and the application of spraying units is described. Malaria is either endemic or hyperendemic in the coastlands, estuaries and in suburbs and periplanetic towns. In the interior it is under-represented and hyperendemic in most communities. The vector *Anopheles darlingi* is widespread and *A. stephensi* was not proved to be transmitters of malaria, but they are potential vectors and possibly maintain small proportions of local malaria. In the north-west where *A. gambiae* appears to be a carrier. These persons with the malaria are replacement and non-domestic and are thus not affected by DDT house spraying.





GILROY A. D. Malaria Control by Coastal Swamp Drainage in West Africa.

This book is reviewed on p. 1043.

SANDOSHAM, A. V. Malaria in Malai. A Handbook for Anti-Malaria Students.

This book is reviewed on p. 1045.

RODMAN J. Contribution à l'étude des Plasmodiums des anthropoïdes africains. Transmission du *Plasmodium malariae* de l'homme au chimpanzé. [Transmission of Human *Plasmodium malariae* to the Chimpanzee.] *Ann. Soc. Belg. de Méd. Trop.* 1948, Mar 31 v 28 No. 1 39-49

The author had previously shown that the quartan malaria parasite (*P. rodhaini*) of chimpanzees was transmissible to man (this *Bulletin* 1943, v 40 438) giving rise to an infection indistinguishable from that caused by *P. malariae*. He now reports the results of the inoculation of human *P. malariae* into chimpanzees. The first attempts were negative but in 1947 three transmission of a strain obtained from Mr P. G. Shute of Horton were successful. 10-15 cc of defibrinated blood containing numerous *P. malariae* parasites were inoculated intravenously into young chimpanzees. The parasites were subsequently found for varying periods in the peripheral blood, augmenting to a crisis when as many as 7000 per cmm. were found in one case. The animals showed no ill-effects from the disease. The infection disappeared spontaneously in one of the chimpanzees, but still continued in a very sparse form in the remaining two. Blood from one chimpanzee at the height of the infection was put back into a human being and gave rise to a typical attack of quartan malaria. The chimpanzee must therefore be regarded as a reservoir of *P. malariae* in Central Africa.

[It is now more than ever certain as a result of these experiments that *P. rodhaini* should be regarded as being a synonym of *P. malariae*.]

P. C. C. Gurnham

RIGBOY R. H. A Consideration of the Use of Blood and Oxygen as Supportive Therapy in the Treatment of Malaria. *Am. J. Cl. Path.* 1948, June v 18 No 6, 485-90 3 figs. 11 refs.]

In various publications since 1941 (this *Bulletin* 1943 v 40 118, 420 1946, v 43 309 630 1947 44 503 853 1035) it has been demonstrated both experimentally and clinically that in acute malaria infections anaemia results from parasite destruction of the red cells and from an anaemia which further decreases their oxygen-carrying capacity. Monkeys infected with *P. knowlesi* at different stages of the infection were treated with oxygen, with immediate and spectacular improvement in their general condition. This improvement lasted while the animals were in the oxygen chamber in spite of the steadily increasing parasitaemia. On withdrawal from the oxygen chamber the monkeys rapidly collapsed. In other cases, entry of the animal into a chamber containing approximately a 40 per cent concentration of oxygen together with quinine treatment was found beneficial. The oxygen served as a supportive measure until the quinine destroyed the parasites. Yet again, combined quinine treatment, transfusions of human blood, and entry into an oxygen chamber greatly prolonged the lives of monkeys moribund from *P. knowlesi* infections.

The blood transfusion and oxygen treatment of malaria is based on sound physiological principles. Capillary occlusion with petechial haemorrhages is found in various organs in *P. falciparum* infection. This is due to a stagnant anaemia with increased permeability of the capillaries which leak their fluid

content into the surrounding tissues, so producing haemo-concentration. Why these lesions should occur in one case in the brain and in another in the lungs or the heart is not known. Nicotinic acid causes dilatation of the cerebral capillaries, and "aids in restoration of respiratory systems", it has been used both alone and in conjunction with oxygen in the treatment of *P. falciparum* infections in man, with rapid relief of symptoms [this *Bulletin*, 1944, v 41, 536, 1947, v 44, 495]. Transfusions, oxygen, and nicotinic acid are only adjuvants to the specific drug treatment of malaria, but they may support the patient until this has time to act.

A R D Adams

VINCKE, I H & LIPS, M. Un nouveau plasmodium d'un rongeur sauvage du Congo, *Plasmodium berghiei* n sp [*Plasmodium berghiei*, a New *Plasmodium* of a Wild Rodent in the Belgian Congo] *Ann Soc Belge de Méd Trop* 1948, Mar 31, v 28, No 1, 97-104, 14 coloured figs on 1 pl

A new *Plasmodium* (*P. berghiei*) from Congo tree rats is described. The rats belonged to at least 5 species, including *Thomomys surdaster*. 14 out of 93 rats showed parasites in the blood. The infection can be transferred with ease to white mice and to rats (*R. r. frugivorus* and *alexandrinus*), in which animals it causes a heavy parasitaemia followed by death between the 11th and 15th days. In inoculated wild rats, the infection as a rule is less severe. There is enormous enlargement of the spleen and liver, which are heavily pigmented. The blood of infected animals shows ring forms usually with one chromatin dot, followed by schizogonic forms. When mature, these divide into 6 to 20 merozoites surrounding a central mass of black pigment. Macro- and microgametocytes are produced, these have fine black pigment and measure 7 to 8  $\mu$  in diameter. The most characteristic features of the parasites are two—the frequency with which multiple infections of the erythrocyte occur and the gross enlargement of this cell. Sometimes six rings are found in a single cell and the cytoplasmic masses are apparently continuous. The absence of pigment is about the only feature which enables such forms to be distinguished from schizonts. The diameter of the rat's corpuscles is normally between 5 and 6.5  $\mu$ , infected corpuscles enlarge to 10.6  $\mu$ . Stippling does not occur.

The insect vector of *P. berghiei* is most probably *Anopheles duren*, common anophelines (e.g., *A. gambiae*) of the region failed to transmit it. Before the discovery of this parasite, *A. duren* had often been found infected with sporozoites in the salivary glands (7 per cent rates). It had been found in large numbers gorged with blood, in the tree canopy of the forest near Elisabethville. The blood was mammalian but rarely or never human, dog, cat or antelope. The authors therefore looked for an animal host prevalent in the forest canopy and they incriminated the tree rats, a successful climax to a very intelligent piece of field work. During the 1947-1948 season, *A. duren* failed to show infections in the glands (out of 1,203 examined) and so far sporozoite transmission from this mosquito to the rat has not been made. Parasites resembling *P. berghiei* have, however, been found in the gut of wild-caught *A. duren*, and in one case the contents of the gut, when inoculated into a white mouse gave rise to a fatal infection due to a parasite apparently identical with *P. berghiei*.

P C C Garnham

RIGDON, R H & ROSTORFER, H H. Observations on the Anemia in Ducks Infected with *P. lophurae*. *Blood* 1947, May, v 2, No 3, 244-55, 5 figs [15 refs]

This paper is written in a confused and, it must be confessed, somewhat confusing manner. Thus, at the beginning of the section "Experimental",

reference is made to figure 1 a demonstrating the parasitaemia and anaemia in a typical malarial infection in a fatal case. The height of parasitaemia is shown in the figure as occurring on the third day yet a few lines below the words quoted above comes the statement "In these ducks the peak of the parasitaemia is reached on the fifth day."

The author's conclusions would appear to be that the anaemia caused by *P. L. pharis* in ducks is due to destruction of mature erythrocytes and the replacement of the latter by erythroblasts which are poor armor of oxygen. The rapid diminution in the number of parasitized cells after the peak of the infection is considered to be due to the fact that the erythroblasts as a class is unsuitable to the needs of the parasite and do not become parasitized.

H. E. Shortt

CINGRICH W. D. Duration of Immunity to Malaria (*Plasmodium culicium*) in the Canary. *J. National Malaria Soc.* 1948, June v 7 No. 2 109-17 6 figs.

This account of the duration of immunity to *Plasmodium culicium* in the canary is based on the reactions of canaries, cured of blood induced infections by anti-malarial drugs, to inoculations of the homologous strain of the parasite.

These inoculations were made at monthly intervals in two series in one of which each bird received 500,000 and in the other 10,000,000 parasites. Controls consisted of (a) birds with latent infections and (b) normal birds.

The conclusions drawn by the author from the experiments were based on three criteria: (a) increasing or decreasing parasitaemia after the first inoculation; (b) the degree of parasitaemia produced; and (c) the duration of the patent parasitaemia.

These conclusions may be summarized by stating that the birds showed a progressive decline in their acquired immunity from the first month after cure until the sixth month with a total extinction of immunity after eight months.

H. E. Shortt

See also p. 983 SMITH STEELE EMMAN & COMBE The Thoracic Distribution of Radioantimony Inhaled as Sulfine.

## BLACKWATER FEVER

TISSEUIL J. La fièvre hémoglobinoque en 1942 dans les troupes stationnées au Soudan, en Guinée et Côte d'Ivoire. *Blackwater Fever in 1942 in Troops stationed in French Sudan, Guinea and Ivory Coast. Bull. Soc. Path. Exot.* 1948 v 41 No. 3 4 173-8

In 1942 there were 98 cases of blackwater fever in a population of about 4,000 Europeans in Central French West Africa. There were no cases among an indigenous population in the same region which numbered about 20,000. Most cases occurred in the second half of the year which was the epidemic season of malaria and most of those affected showed some form of active employment. Blackwater fever was common among those who were in the habit of treating themselves with quinine during an attack of malaria. In 1942, quinine was used as a suppressant during the first half of the year and prophylactic during the second half. Quinine was used throughout the year in small isolated posts. A later survey was however apparently taken only in the districts the maximum incidence of blackwater fever was recorded during the first half of the year when quinine was being taken. In the second half

of the year when prémaline was distributed the number of cases was reduced, especially where the drug was correctly taken. Thus, in Camayenne near Goléah and Konakry, malaria was as severe as in neighbouring areas, but in 70 Europeans there was not one case of blackwater fever. In this district prémaline was taken correctly, while in Goléah, where quinine was being administered, two Europeans out of five developed blackwater fever.

Blackwater fever during 1942 was very severe. Out of a total of 37 deaths among Europeans, 28 were due to it. Classical treatment was not very effective, the death rate ranging from 15 to 35 per cent. Attempts to prevent development of blackwater fever included monthly systematic splenic examinations of all Europeans. All those with palpable spleens were given the following treatment—quinine 1 gm daily for 2 days, quinine 300 mgm daily for 5 days. The taking of suppressive drugs daily was insisted upon and maintenance of drug suppression was ordered for 15 days to three months after the subject left the endemic area.

B G Macgrath

LEFROU, G. Considérations sur l'étiologie de la fièvre bilieuse hémoglobinurique à propos de 123 cas observées au Soudan. [Observations on the Aetiology of Blackwater Fever, arising out of 123 Cases in French Sudan. *Bull Soc Path Exot* 1948, v 41, Nos 3/4, 176-87.]

This is an account of the results of an enquiry which originated as a result of the unusually high incidence of blackwater fever in French Sudan during 1942 and 1943. Most of the cases referred to were treated in hospital at Bamako and this study, together with previous records, covers 82 patients from 1943 to 1946 including 72 males, 10 females, 6 were children from 2 to 10 years of age. The incidence of blackwater fever was seasonal, the maximum number of cases occurring during the warm rainy period, particularly in September when *P. falciparum* malaria was most prevalent. Cases were very rare during the hot dry season. Of 100 cases investigated, 20 had lived in the district for one year, 39 for two, 22 for three and 19 for four or more years. The author concludes that there is no obvious relation between the length of stay and the onset of blackwater fever. There were 8 subjects who developed blackwater fever within the first six months of their tour, all of whom had lived previously in Africa. Three cases occurred among new arrivals in Africa within the first year. The severity of the attack increased with the length of stay, the mortality after three or four years being considerably higher than that after one or two years. Over the period discussed there were only six recorded cases of blackwater fever in Africans.

Since the introduction of controlled suppressive antimalarial drug treatment blackwater fever has become rare in French Sudan. The abrupt rise in incidence in 1942 was probably related to irregular quininization, resulting from difficulty in obtaining supplies in that year. The author emphasizes the danger of prescribing or taking quinine indiscriminately and irregularly. Blackwater fever developed in some cases during the administration of quinine either orally or parenterally for the treatment of a current attack of malarial fever. It was never observed in those taking regular quinine prophylactically. Haemoglobinuria sometimes appeared in persons suffering from malaria who have never taken quinine, e.g. in members of the indigenous population. The author includes chilling, and emotional disturbances as predisposing factors.

B G Macgrath

MACGRAITH B G. The Syndrome of Renal Anoxia in Malaria and Blackwater Fever. *In Inst Med Trop* Lisbon 1947 Dec v 4, 427-45, 1 fig, 33 refs. A lecture given at the Institute of Tropical Medicine, Lisbon.

## TRYPANOSOMIASIS

EAST AFRICA HIGH COMMISSION Fauna of British Eastern and Central Africa.  
 Proceedings of a Conference held in Nairobi on 24th and 25th May 1947  
 Paper No. 1 74 pp. 1 folding map. 1948. Nairobi Govt Printer  
 [Sh. 2.50]

The conference appears to have limited its discussion almost entirely to the large mammalia often described as "game" the case for conservation and measures for increasing and maintaining a stock, and also the medico-veterinary objections to game animals as spreaders of infections were fully considered. It is clear that the members of the conference were able to take broad and well-informed views on a very complex matter. The members of the conference which was called by the East African Governors Conference represented British Commonwealth territories from South Africa to the Sudan.

The proceedings give an impression that a serious attempt has been made to collect facts and to consider them. But as each Government submitted a statement beforehand, and also published its comments on the resolution passed at the Conference it is not easy to obtain a consecutive picture of any topic the same subject recurs at intervals.

Turning to matters of direct interest to readers of this *Bulletin* we should quote two of the resolutions which were adopted.

3-*Fauna Tsetse Fly and Trypanosomiasis*

"The Conference recognized that under conditions which prevail in Southern Rhodesia the eradication of fauna is a proved method for getting rid of *G. morsitans* but not of other species of tsetse fly which in many cases are of equal or greater importance. This method of fauna destruction should, therefore be tested under more varied conditions at least until other methods of getting rid of *G. morsitans* are available. Experiments now in progress or planned, such as discriminative clearing of bush controlled burning, bush, and large scale application of insecticides may provide alternative and better methods.

The Conference emphasized (a) that since the clearing of fly is of little value unless full use is made of the land cleared plans for efficient land use should be worked out before measures for the eradication of fauna and fly are undertaken, (b) that uncontrolled and unsupervised slaughter of fauna is of little use because the animals are reduced thereby to an insignificant degree. Consequently the destruction of game must be undertaken by experts under proper control, that is, under the aegis of game departments.

4-*Fauna and Animal Disease (other than Trypanosomiasis)*

In view of the part played by wild animals in the spread of diseases of domestic species (rinderpest foot and mouth disease East Coast fever anthrax African swine fever mangle and rabies) etc. provision should be made for veterinary control of game areas either by very close co-operation between Game and Veterinary departments or by placing the management of game departments or the staff of national parks.

"In order to limit the spread of disease by wild animals game reserves, national parks and other game areas should be isolated where or feasible so that movement of the larger species especially ruminants from one game area to another could be prevented.

In the Appendixes E. B. W. KILGUS, Secretary to the East African Governors Conference, discusses what should be the policy with regard to wild animals in view of the increasing human population and urges that game departments should be called upon to be able to make a detailed study of the animals. A. A. DIXON, General Manager of the Rhodesia

Tsetse Flies to Game " H FAIRBAIRN emphasizes the view that game is a reservoir for *Trypanosoma rhodesiense*, and again sets out the evidence Sir Guy MARSHALL states the contrary view

A map, extending from the Sudan to Southern Rhodesia shows National Parks (existing or proposed), Game Reserves and controlled areas The area at present reserved is just over one million square miles, 6.9 per cent of the total area of the British territories P A Buxton

BRITISH MED J 1948, June 26, 1249 Tsetse Fly Problem in Africa Stephen Paget Memorial Lecture [Buxton, P A]

In this lecture, Buxton sums up on broad lines the knowledge that has been gained on tsetse flies and means of controlling them For control of water-side tsetse hand-catching and clearings of various kinds are important, the successful experiment at Anchau (Nigeria) is a pointer to probable future effort For the game flies clearance of vegetation, destruction of game, and human settlement in cleared areas have their place Insecticides might be effective in small areas, but could hardly be applied over large tracts of land The lecture is a conspectus and an opinion, Buxton has returned from several journeys through Africa feeling reasonably optimistic about the tsetse situation Charles Wilcocks

NASH, T A M Tsetse for Tyros 18 pp, 2 pls Medical Department, Nigeria 1948 Lagos Govt Printer

Dr Nash has written this little booklet in very simple English He hopes it will be understood by Africans with educational qualifications as low as Middle II Some parts are useful to doctors, veterinary officers and others interested in tsetse flies He describes first how flies of the genus *Glossina* may be distinguished from other flies, and then gives the characters for the recognition of the different species found in Northern and Southern Nigeria The life history of the tsetse is described and clear instructions are given for collecting adults and pupae There is also a brief account of different types of vegetation and methods of control, and some hints on how to avoid being bitten The two plates illustrate the fly, its antennae, the pupa and the abdomens and hindlegs of *Glossina palpalis*, *G. tachnoides*, *G. morsitans* and *G. fuscica* H S Leeson

RAMOS A S & ASSOREIRA M Aracnoidite opto quasmática tripanosômica e tratamento cirurgico Contribuição para o estudo da cegueira da doença do sono [Optic Chiasma Arachnoiditis in Trypanosomiasis and its Surgical Treatment A Study of Blindness in Sleeping Sickness] An Inst Med Trop Lisbon 1947, Dec v 4, 33-47, 2 figs on pls [11 refs] English summary

WEURMAN C Investigations concerning the Symbiosis of Bacteria in *Triatoma infestans* (Klug) Reprinted from *Antonie van Leeuwenhoek* 1946, v 11, 129-38 1 fig [10 refs]

MEYER H & XAVIER DE OLIVEIRA, M Cultivation of *Trypanosoma cruzi* in Tissue Cultures a Four-Year Study Parasitology 1948, July, v 39, Nos 1/2, 91-4, 17 figs on 2 pls

*Trypanosoma cruzi* has been cultivated by the tissue culture technique by various workers, but the present account describes what is probably the most comprehensive study of *T. cruzi* on these lines The method employed was Carrel's hanging drop technique

Several interesting observations are made among them the curious fact that although the organism was easily maintained in tissue culture in chick embryo material over a period of more than two years yet living chicks could not be infected with the cultures. Other observations were that the entire cycle—trypanosome, leishmania form enthalia and back to trypanosome—took place in one cell and the number of trypanosomes produced was proportional to the size of the host cell. No division of adult trypanosomes was observed nor any indication of sexually differentiated forms. [The paper is evidently a condensation of a great deal of original observation which would repay fuller description.]

H. E. S. 2

## LEISHMANIASIS

GIRAUD P. BERNARD R. & BERGIER P. Chronique du kala-azar à Marseille (A Review of Kala Azar in Marseilles.) *Bull. et Mém. Soc. Méd. 113<sup>pt</sup> de Paris* 1947 Vol. 3/4 612.

In 16 years up to 1939 the authors recorded 165 cases of leishmaniasis in the Marseilles area. In the 8 years 1939-1948 they have found 73 more giving a total of 238. The average number of cases annually for the two periods was thus about the same.

The yearly incidence for the years 1939-1948 is given in a table and shows a sharp drop in 1942-1944 which years only averaged 3 cases. This was followed by a brisk rise in 1945-1948. The authors have not entirely satisfied themselves as to the exact cause of this change. No doubt the dry years 1943 and 1944 were unfavourable to the breeding of the insect vectors and the rainy years 1945 and 1948 (when there were 16 and 17 cases) were favourable to such breeding. The disappearance of many dogs during the wartime period of food shortage would not be sufficient to explain the change in incidence. The authors, however, noted a comparable situation in the endemic zone observed between 1930 and 1935 when there was a similar variation with a maximum of 4 cases in 1932.

Over half the patients were under 3 years of age and the incidence fell rapidly after 4 years. Three cases were in infants under 10 months and only one in an adolescent and two in adults. Infection occurred regularly in the suburbs and country districts. Two cases originated in Corsica.

The topographical distribution and incidence in dogs corresponded closely with that in man over the same period. (Land juncture (doubtful) was simple and reliable in dogs see also this *Bulletin* 1948 45 803).

The authors believe on epidemiological grounds that the local endemic is essentially a disease of dogs accidentally transmitted to man by tick rather than by *Phlebotomus* and that in general it is endemic in the French Mediterranean area. It is a constant and stable. It added that two children with kala azar also had histrelymphatic leishmaniasis. H. J. O. D. B. 100 1947

RACHMILEWITZ M. BRAH J. & F. VAIT A. Hematologic Observations in a Case of Kala-Azar. *Bh. J.* 1947 July Vol. 4 361 5 115, 1 ref.

"The hematologic findings in case of kala azar under the influence of peptic treatment are described. The type of the anemia the leucopenic bone marrow the increased uric acid in spite of treatment, and the subsequent changes following treatment strongly suggest increased red cell destruction most probably by phagocytosis as the cause of the anemia.



DE AZEVEDO, J F, TEIXEIRA, A W G & COITO, A de M F Sobre a infestação por leishmanias nos cães de Lisboa [Leishmania Infection in Stray Dogs in Lisbon] *An Inst Med Trop* Lisbon 1947, Dec, v 4, 99-106

The English summary appended to the paper is as follows —

"As a complement to the studies carried out in the Institute of Tropical Medicine on the epidemiology of the kala-azar, the authors have determined the rate of infestation by leishmaniae in vagrant dogs of Lisbon

"For this purpose, from 1945 to 1947, they searched for leishmaniae directly in spleen, as well as in liver smears of those animals, by culture of these organs (medium NNN) and in bone marrow and nasal mucus smears

"Out of 137 dogs examined, 9 have been found infected, which gives an infection rate of 6.5 per cent, a percentage considerably higher as compared with those of 3.6 and 2.08 per cent found by other investigators also in dogs of Lisbon in the periods of 1910-1912 and 1936-1938 respectively. In one of the dogs leishmaniae have been found in the nasal mucus

"They also observed that the largest proportion of infected animals was found among the oldest dogs and that the infection rate in the females was larger than that of the males"

SMITH, R E, STEELE, J M, EAKIN, R E & COWIE, D B The Tissue Distribution of Radioantimony Inhaled as Stibine *J Lab & Clin Med* 1948, May, v 33, No 5, 635-43, 7 figs

BRADY *et al* [this *Bulletin*, 1945, v 42, 747] studied the fate of radioactive trivalent antimony in dogs after intravenous injection. The inhalation of stibine ( $SbH_3$ ), a gaseous trivalent compound of antimony, was shown by the present authors to cause reduction in the level of parasitaemia of chickens infected with *P. gallinaceum*. This substance containing the metal in radioactive form has now been used to determine the concentration of Sb in the blood and tissues of normal and infected chickens as well as in guinea-pigs at various time intervals after administration.

The antimony isotopes were prepared by bombardment in the cyclotron and the two forms produced with a half life period of 2.8 and 60 days respectively were used as a mixture for the production of stibine by the action of HCl on the fusion product with magnesium. The animals were exposed to various concentrations in a special chamber for different periods and on removal were bled prior to removal of tissues for estimation of antimony. The radioactivity of samples was measured by means of a beta ray counter under standard conditions and the amount of Sb determined with reference to standards. The concentration of stibine in the chamber was approximately 25 parts per million and the time of exposure about 50 minutes.

Haemolysis of red blood cells occurred in some cases. The results obtained with chickens heavily infected with *P. gallinaceum* were not significantly different from those with controls. The concentration of Sb in the blood stream fell off gradually but more rapidly in guinea-pigs than in chickens. At first there was some localization in red cells but the excess of metal over that in plasma was reduced with time. The concentration in most tissues approximated to those in blood, but in liver and spleen there was a maximum level about 1 hour after treatment, and after four hours the level was higher in liver, spleen and kidney than in whole blood. Antimony appeared to be eliminated at a greater rate by the guinea-pig than by the chicken.

J D Fulton

## FEVERS OF THE TYPHUS GROUP

RABLOWITZ, Esther, WEINER, M. & GROSSOWITZ, N. Cultivation of *Rickettsia prowazekii* in Dead Chick Embryos. *Proc Soc Exper Biol. & Med.* 1948, Apr., v 67 No. 4 469-70

Living cells were still present in chick embryos 18 days after the latter had been killed, on the third day of development, by chilling at 4°C. for 4 hours and then kept even at a temperature of 37°C.

Rich cultures of rickettsiae were found after 14 days of cultivation in embryonated eggs killed by chilling and inoculated within about seven days. Storage was at room temperature.

Successful cultivation was obtained with rickettsial suspensions containing too few organisms to yield cultures when the usual technique was adopted. The special advantage of the method is that the killed embryos can be stored "for some time" and then used like ordinary culture media. The eggs can be inoculated in the field and transported to the laboratory without the special precautions that are needed when living embryos are employed.

John B. D. Macgregor

CLARKE, Delphine H. & FOX, J. P. The Phenomenon of *in vitro* Hemolysis produced by the Rickettsiae of Typhus Fever with a Note on the Mechanism of Rickettsial Toxicity in Mice. *J. Exp. Med.* 1948, July 1 v 83, No. 1 3-11 [12 refs.]

Suspensions containing sufficient numbers of *Rickettsia mooseri* or *R. prowazekii* especially when prepared from yolk-sac cultures were found to cause haemolysis *in vitro* of red blood cells of rabbits and sheep but not of mice, cotton rats and guinea-pigs. Suspensions of *R. orientalis* did not haemolyse rabbit cells.

The haemolysis was closely associated with the bodies of living rickettsiae being present in the sediment obtained by high-speed centrifugation but not in the supernatant fluid—it was destroyed by formal (0.5 per cent) and by heating to 56°C. for one hour. Its activity in suspensions was parallel with the toxicity for mice and the infectivity for cotton rats of the suspensions.

It is thought likely that the degree of haemolytic activity may turn out to be a rapidly observable though only roughly quantitative index of the infectivity of suspensions. Homologous antisera inhibit the haemolytic action which therefore may form the basis of a useful serological test having the special feature of depending on a property of living rickettsiae. The haemolytic factor may possibly be identical with the rickettsial toxin which is known to cause early death in experimental mice.

John B. D. Macgregor

SANDOR, G., GIROUD, P. & SKORISNY, C. Mlle. Etudes des anticorps anti-rickettsiaux du serum de lapin. [Study of Rickettsial Antibodies in Rabbit Serum.] *J. de l'Ass. Pasteur* 1948 June 74 N. 8 518.

In a previous note (*this Bulletin* 1948, 45) the authors discussed the identity of the antibodies produced in rickettsial antiserum and they now present the first results of the application of their technique in distinguishing the antibodies in rabbit serum.

As in the case of normal rabbit serum, efficient precipitate cannot be extracted by simple dialysis when distilled water is used. Any rat of Indian origin is prolonged for only 2 or 3 days. Acidic water (pH 5.5) on the other hand makes it possible to obtain abundant precipitate from dialysed serum diluted one in four. This precipitate accounts for an  $\alpha_2$  of 0.8

per cent of the serum proteins and can be separated into an insoluble and a soluble protein fraction in about equal parts, in the presence of a dilute phosphate buffer (N/100) at about pH 6 these are euglobulin II B and II A.

The insoluble fraction disperses with difficulty and only in weakly alkaline medium, producing a markedly opalescent suspension. It represents a lipoprotein complex containing about 40 per cent of lipids consisting entirely of neutral fats. This fraction is devoid of any agglutinating power against rickettsiae.

The soluble protein fraction contains only a small percentage of lipids and gives a completely clear solution. It often accounts for all the agglutinating activity, but a small but variable proportion of this is also present sometimes in the pseudoglobulins.

In rabbit anti-ovalbumin serum or horse antiglobulin serum there is a euglobulin I which contains a small amount of the specific flocculant factor, but the greater part is to be found in the pseudoglobulins. Common proteins are close to rickettsiae antigenically, but viruses differ in this respect. Rickettsiae may be regarded as being comparable with endotoxins or bacterial antigens. Similar results were obtained with STEFANOPOULOU in the case of yellow fever antiserum in the horse.

H J O'D Burke-Gaffney

GAASE A Die Thermostabilität der Agglutinine in der Differentialdiagnose von Fleckfieber und Proteusinfektion [The Thermostability of Agglutinins in the Differential Diagnosis between Typhus Fever and Proteus Infections] *Ztschr f Hyg u Infektionskr* 1948, Apr 1, v 127, Nos 6/8, 730-41, 10 figs [21 refs]

Contrary to the findings of some previous workers, the author has found that the agglutinins against *Proteus OX19* are very variable in their resistance against heating. He tested the sera of 220 typhus patients before and after heating to 56°C for one hour, and found that although heating caused a fall in the Weil-Felix titre in 79.5 per cent there was no change in 13.2 per cent and there was actually a rise in 7.2 per cent. In 68.6 per cent of the cases, the titre after heating remained at a height of 1-100 or over.

In a case of furunculosis due to *Proteus vulgaris*, the patient's serum did not react to *Pr OX19* neither did the serum of any of 10 guinea-pigs which had been immunized against 10 different strains of *Pr vulgaris* although several of these strains were agglutinated by the sera of typhus patients. These findings are regarded as additional evidence of the specificity of the Weil-Felix test for typhus fever.

The agglutinins of the above guinea-pigs against homologous strains of *Proteus* organisms showed a higher average degree of thermostability than was shown by the agglutinins of typhus patients against *Pr OX19*, yet there was a fall in the titre in 13.9 per cent of the cases after heating, so that the thermostability of the agglutinins in the Weil-Felix reaction cannot be regarded as supporting the diagnosis of *Proteus* infection as opposed to that of typhus fever.

Joh W D Mignaw

BRIOT J & MATHIEU R Diagnostic du typhus par réaction de fixation du complément. Etude de divers antigènes. The Diagnosis of Typhus Fever by the Complement-Fixation Reaction. A Study of Various Antigens. *Bull Soc Path Exot* 1948, v 41, Nos 3/4, 112-14.

In a trial of various antigens prepared from typhus vaccines the best results were obtained with a formalized vaccine of the Durand Groux type, preferably less than one year old.

One team consisting of a sanitary inspector and a nurse working 8 to 10 hours a day can do an average of 17 residences giving 107 treatments and examinations without examination the team can do 180 people per day. The treatment costs very little and takes - 25 ounces of 10 per cent. DDT for one person and his bedding, etc., and one ounce of phenyl cellosolve lotion per woman and 0.5 oz. per man.

No toxic effects were observed among the treated persons or the operators.  
H. S. LECHE

ESKAY, C. R. & HENKEL, F. M. Relation of Reported Cases of Typhus Fever to Location, Temperature, and Precipitation. *Pub Health Rep Wash.* 1948 July 18: 63 No. 29 941-8 4 figs.

Most of the information contained in this survey of the incidence of murine typhus fever in the U.S.A. is presented in the form of graphs and a map. The total number of cases reported during the period 1913-1944 was nearly 33,000 of which almost 95 per cent. occurred in the southern States.

Owing chiefly to the increasing recognition of the disease 60 per cent. of the cases were reported in the last six years of the above period. [The statement in the body of the paper that 60 per cent. of all the cases occurred during the 31 year period is obviously due to a typographical error.]

The disease is concentrated in the zone between 31° and 33° north latitude especially towards the south of the zone. Fewest cases occurred during the winter and spring months. August, July and September were the months of highest prevalence. The number of cases reported annually increased every year except in 1940 when the number was smaller than in 1909. This departure from the trend is regarded as being due to the exceptionally cold weather experienced in January 1940. There was no significant degree of association between rainfall and rate of incidence. JOHN W. D. M.

CAILLON, J. & VANDERLEY, R. Essais d'action enzymatique sur des micro-organismes du groupe des Rickettsias. [Studies on the Action of Enzymes on Rickettsias.] *C.R. Soc Biol* 1948 Mar 14, Vol. 5 A 3rd-7

The authors have applied a method called *enzyme analysis* to the study of the cytological structure of rickettsiae. The method has already been employed in the investigation of bacterial cells by H. I. I. whose paper on the subject was still in the press at the time of writing.

Rickettsial smears were fixed in absolute alcohol, then treated for varying periods up to two and a half hours by solution of one of the two enzymes, ribonuclease and deoxyribonuclease. The smears were washed and stained by Giemsa's stain.

Striking results were obtained by treating the smears with the latter enzyme especially in the case of *Rickettsia psittaci* obtained from the ovaries of infected *Coturnix* f. *psittaci*. After prolonged application the rickettsiae failed to take on the stain.

Smears of *R. mooseri* from infected guinea-pigs were also affected though to a lesser degree but they had not been freshly prepared.

The findings were regarded as supporting the view that rickettsiae are intermediate in structure between bacteria and filterable viruses.

Reference is made to the work of T. A. K. et al. *Nature* 1946 Dec 21 917, who have found that the chemical composition of *R. psittaci* intermediate between that of bacteria and viruses. JOHN W. D. M.

PHILIP, C B Tsutsugamushi Disease (Scrub Typhus) in World War II. J  
Parasitology 1948, June, v 34, No 3, 169-91, 1 map [30 refs]

This paper consists chiefly of a critical review of the new knowledge of tsutsugamushi disease gained in the course of the Asiatic-Pacific campaign of 1941-1945. Most of the papers referred to by the author have been dealt with in this *Bulletin* and as the article is a summary it does not lend itself to the preparation of an abstract.

A few points of special interest are as follows—The allied forces escaped several major disasters solely because there did not happen to be any action by the enemy at the times and places of occurrence of large outbreaks of the disease, and it was only because of the prompt and energetic action taken by the allied experts to discover and apply effective measures of control that serious interference with the campaign was avoided.

Although the closely related *Trombicula akamushi* and *T. deliensis* are the only proved vectors of the disease, about 100 new species of Trombiculidae ("cligger mites") have been discovered since 1940—mostly in the Eastern Hemisphere. Despite numerous references in the literature to "blood meals" the larval mites do not ingest blood, but only lymph and tissue fluids. The larvae do not remain attached to the animal hosts for more than three or four days, so that they have never been found attached to the subsequent eschars on patients.

The chief reservoirs of infection of the mite-borne, as of the tick-borne, fevers of the typhus group are believed to be the arthropod vectors, the vertebrate hosts are now regarded as being transitory reservoirs.

The correct nomenclature of the agent is discussed, the name *Rickettsia orientalis* was first applied in 1930, by Nagayo *et al* who had also referred seven years earlier to its apparent rickettsial relationship. The author, however, considers that the name *R. tsutsugamushi* "will be most generally adopted" for the following reasons—(1) Hayashi, in 1920, described a protozoon which he called *Theileria tsutsugamushi*, as the cause of the disease, (2) Various Japanese writers have stated that Hayashi "must have seen rickettsiae in some of his 1920 preparations" so that his specific name by generic transfer deserves acceptance. [Yet the earlier name *Rickettsia nipponica* applied by Sellards is considered inadmissible because its sponsor wrongly reported that he had cultivated the agent.]

The author refers to the pseudo-typhus of Sumatra like most other workers he has overlooked the fact that the disease referred to should be called pseudo-typhoid when translated into English.

The very puzzling differences in the antigens of various strains of the agent are discussed and mention is made of a patient whose complement-fixation titre against a New Guinea antigen was 1-512, whereas against a Burmese antigen the reaction was negative.

A useful map dated 1946 shows the known geographical distribution of mite typhus.

Apart from the influence of combat fatigue and other depressing factors, which caused an increase in the fatality rate, there was evidence of astonishing differences in the virulence of the infection in various localities, for example among 1 469 cases at Owi Brik the fatality rate was only 0.6 per cent, but in smaller outbreaks in Goodenough Island and Finchhaven the rates were 27.5 and 35.3 respectively despite hospital care and the absence of adverse conditions.

A bibliography described as partial contains 30 references. In this short paper of 23 pages the author has succeeded in presenting a clear description of the special features connected with the epidemiology and control of the disease as observed during the second world war.

JOHN H. D. MCGAW

SHEPARD C. C. & HUTTENNER R. J. Q Fever in Los Angeles County. Description of some of its Epidemiological Features. *Amer J Pub. Health*. 1948 June v 38 No. 6 781-8.

By this careful epidemiological study the authors have confirmed and extended the findings of previous workers in the U.S.A., but although the disease in man seems to be definitely associated with contact with cattle the mode of transmission, especially to the infected cattle remains a matter for speculation. Proof is still lacking that human infection is acquired from cattle the authors think it possible that cows and human beings may be infected from a common source.

No evidence of transmission by ticks has been found in any of the American outbreaks.

The authors investigated 17 cases which occurred within 10 to 30 miles of the City of Los Angeles in an area in which there were large numbers of dairies where the cows were kept continuously in pens because of the lack of pasture. Eleven of the cases occurred within a period of seven weeks during April and May 1947. The usual hospital diagnosis was atypical or virus pneumonia pneumonia was detected in all the cases investigated by X rays. The complement fixation titre reached a height of 1-64 or over in every case and *Rickettsia burnetii* was isolated from four patients by guinea pig inoculation.

All but two of the patients had either visited dairies or had lived near them, though none had been employed in a dairy or had immediate contact with cows.

Sera of 20 dairy workers in the area were tested. ten reacted at titres of 1-4 to 1-32, though none gave a history pointing clearly to the previous occurrence of an attack of Q fever.

Sera of 163 other persons living in the area, but not connected with the dairies were tested. five reacted at titres of 1-4 to 1-16.

Sera of 93 persons living in the District of Columbia were all negative. Sera of 130 cows from nine dairies in the area were examined. 21 were positive ten of them at titres of 1-64 or over.

The findings suggest that Q fever usually in a mild form, frequently occurs among the cattle dairy workers, and residents near the dairies of the area.

In an Addendum it is stated that since this paper was submitted for publication HUTTENNER *et al* have reported the finding of *R. burnetii* in raw milk from four dairies in South California [see this Bulletin 1948 v 45 469]. The authors of the present paper were also two of the four authors of the above-mentioned report].

John W. D. McGraw

## YELLOW FEVER

CALLEY O. R. LAEMBERT H. W. Jr & HAYES G. C. The Home Range of Brazilian Cebus Monkeys in a Region of Small Residential Forests. *Amer J Hyg* 1948 May v 47 No. 3 314-14 3 figs.

Jungle yellow fever in Brazil appears either in an enzootic form in the tropical rain forests or an epizootic form in patchy wooded areas of the central and southern regions. Because no evidence had been obtained that the birds or some species of bats are responsible for the spread of the virus over patchy wooded country during epizootics the present investigation of the role of sylvan primates was undertaken.

The region chosen for study was a 1000-acre Minas Gerais, which lay in the path of an epidemic which during the periods from 1934-1940 was a south-western watershed. A similar pandemic occurred in 1944 which began to

retrace the path followed 10 years previously. A field laboratory was, therefore, established in front of the epidemic with the intention of imitating investigations before the virus actually arrived.

The country around Passos is characterized by large open pastures. The forested areas are for the most part limited to the steeper hilltops and deeper ravines, where may be found the remnants of climax and young-type forest. These wooded areas are frequently isolated from one another by one or two kilometres of pasture or they may be connected by marginal growth along streams.

During the study, which lasted 15 months, 1,025 monkeys were captured. 62 per cent were taken more than once. Only one animal was found more than 1,000 metres from his home forest and less than 3 per cent of recaptured specimens were known to have travelled distances of 100 to 800 metres across open country.

In a large forest, where there was a number of bands of *Cebus* monkeys, it was rare to find one band wandering into the territory of another.

Thus, the normal movements of *Cebus* monkeys do not appear to explain the rapid and extensive spread of yellow fever through the sparsely wooded areas of central and south Brazil.

F O MacCallum

## DENGUE AND ALLIED FEVERS

MCCARTHY, D D & WILSON, D Bagster. Dengue in the East African Command Incidence in relation to *Aedes* Prevalence and some Clinical Features. *Trans Roy Soc Trop Med & Hyg* 1948, July, v 42, No 1, 83-8

This paper deserves attention because of the emphasis laid by the authors on the extreme variability of the manifestations of dengue, a feature which they rightly regard as being responsible for frequent failures to recognize the disease. Only occasional cases had been previously diagnosed in the civilian hospitals of British East Africa, and in the Command itself the diagnosis was rarely made except when an epidemic occurred.

The disease was specially prevalent in Dire Dawa and Harrar in Ethiopia, Mogadishu in Somalia, Diego Suarez in Madagascar, and Mayotte in the Comoro Islands. Cases also occurred in other places in Somalia, in British Somaliland, at Mombasa, and in Mauritius.

At Diego Suarez, the incidence among European units in 1943 was more than 100 per cent, but the rate for all races was only 12.3 per cent. The difference in incidence is attributed to difficulty in recognizing the rash and other features of the disease among Africans. [No mention is made of the probable influence of immunity resulting from previous attacks.]

At Diego Suarez in 1942 many cases were diagnosed as sandfly fever, although *Phlebotomus* was completely absent from the area here and at Mogadishu the French and other residents regarded the yearly outbreaks as due to influenza. Severe pains did not occur. A rash, sometimes lasting only one or two hours, was seen in nearly half of the European patients, but a fully developed rash, rubeoloid or an erythematous background, was seen in only 20 per cent. Dusky redness of the fauces and palate was frequently seen. An alteration of the sense of taste was common, and in some mild cases was the only symptom of which the patients complained.

In 25 per cent of the cases one lymphatic gland or one group of glands was enlarged. Generalized lymphadenitis was never seen. Typical saddle-back

temperature charts formed only 10 per cent. of the total continued, remittent and intermittent types of fever were equally common. A fall of temperature by crisis was the most constant feature of the illness. The pulse was about 100 per minute at the onset soon the rate fell to about 70.

Leucopenia was usually pronounced by the 4th day.

The disease is described as being amazingly variable in its clinical manifestations, with no predominant symptom recurring as characteristic, each symptom taking its turn as the dominant feature.

At Mogulishu the reduction of the *I* *les* index from 77 per cent. to 10 per cent. caused almost complete control of the disease. At Diego Suarez, control was not effective till the index fell below 2 per cent.

Joh W D M 13

## PLAGUE

SANDOR G. GIRARD G. & SKROBISZ, C. with the collaboration of A. CHEVALLIER. Etude du serum antipesteux de cheval. [Study of Plague Antiserum in the Horse.] *Ann. Inst. Pasteur* 1943, June v 74 No. 6 516-17.

The authors have previously shown that the plague bacillus does not possess a true exotoxin [this *Bulletin* 1947 v 44 100]. The present note brings the matter farther in discussing a study of the antiserum produced by the injection of plague bacilli of 1 vol. While *P. pestis* contains purely protein antigens which are chemically related to exotoxins, it is shown on immunological grounds from the behaviour of the euglobulin fractions produced that plague antiserum is of the antibacterial and not of the antitoxic type. A. Chevallier and a co. (Brit. J. Exper. Path. 1948 19 44) have shown antiserum resistant proteolysis in a weakly acid medium, followed by selective coagulation. In plague antiserum this resistant fraction is absent. The antigen of *P. pestis* is not exotoxins or true toxins but simply bacterial antigens.

H J O'D Burke-C. 11/1/48

CHARARD, A. G. Les arthropodes vecteurs de la peste bubonique. [Arthropod Vectors of Plague.] *Bull. Mus. Hist. Nat. Comp. Paris* 1947 v 22, Nos. 3 & 4 53, 189-200 357-9. Numerous refs.

The Indian Plague Commission of 1907-1911 confirmed the findings of the Royal Plague Commission of 1898 previous workers, and subsequent workers that plague was transmitted to man by fleas of the domestic rat. The problem has widened considerably since these fundamental investigations were carried out and especially with the introduction into it of viral plague and its diagnosis. The author has compiled reference work of great utility. He puts forward as a possibility in the epidemiology of plague three distinct cycles: (1) in wild rodents, (2) in domestic rodents, and (3) in man alone.

The first article deals only with wildulent viral plague. A wealth of information on host species, geographical vector, etc., together with references to authority is given in a table listing also the wildulent species. Besides rodents a number of wild animals are attacked by plague among the primates and *Remousopneustes* and *Salmonella*. The siphonophore parasites of the rodents are all listed in the table. A considerable list, with details of efficiency of transmission precedes the table and represents much labour.



In the second article dealing with the domestic rodent cycle and the human cycle, the same careful treatment is followed. A second table is given under the heading "spontaneous or experimental infection and experimental transmission of plague by fleas", with columns for species (71), chief host, spontaneous or experimental infection, experimental transmission and authority.

In his summary, the author concludes that "an arthropod can be efficient in the transmission of plague from one *Citellus* to another but incapable of transmission to an animal of another group". "It is now recognized that all the siphonaptera can become plague infected, but are often described as not pestiferous". In no case, however, has the author found a flea incapable of transmission where the following were fulfilled (1) a good crop of fleas (2) The use of the host preferred by the insect. Anatomical considerations may also play a part in transmissibility of plague.

This work is very systematic, and comes from, and with the authority of, Brumpt's Institute in Paris  
W F Harvey

TOUMANOFF, C & HÉRIVAUX, A. La nature du sol et le stationnement des puces (*X cheopis* et *X astia*) Essai d'interprétation [The Nature of the Soil and the Habitat of Fleas] *Bull Soc Path Exot* 1948, v 41, Nos 3/4, 293-300 [12 refs]

It is well known that fleas may survive in rat burrows under conditions which, as judged by the general climatic conditions, should have proved lethal. That is easily explained by the fact that climatic conditions inside sheltered places, burrows, cracks and crevices are not the same as those outside. This has led the authors to plead that in the ecology of insects there is a distinction between ecoclimate, a summation complex of meteorological factors, and the "microclimate" which may determine the prevalence or preponderance of a flea-species. The same distinction is to be found in the use of terms like site and "micro-site". In this study two closely allied species of fleas are contrasted, *X cheopis* and *X astia*. The soils or dust and refuse, which experience had shown could be called *cheopis* soils and *astia* soils were analysed and showed a well marked difference. *Cheopis* soil was sandy clay, impermeable to or retentive of water, while *astia* soil was purely sandy. Chemical analysis naturally showed the former to have a high content of colloidal alumina and the latter to have more colloidal silica. Little difference between the pH of the two soils was demonstrable—5.05-5.39.

An old observation of Hirst had emphasized the difference in temperature requirements for the habitat of the two flea species, lower for *X cheopis* than for *X astia*. The question arose therefore whether the chemical characters of *cheopis* and *astia* soils were simply physical and not nutritional requirements, not even a matter of humidity *per se*, but the physical fact that evaporation of water leads to lowering of temperature. This seems to be the opinion, not absolute of course, of the authors themselves.  
W F Harvey

HOPKINS, G H E. Rats, Fleas and Plagues in Uganda. 54 mimeographed pp., 22 tables & 2 folding maps [23 refs] Published by permission of the Director of Medical Services, Uganda [Undated]

The text of this report, called a reconnaissance report by the author, may be read with pleasure in its entirety. It is permeated throughout by scepticism, by argument on spurious correlations and by the production again and again of the "negative instance". Nevertheless sharp, crisp well-argued conclusions are drawn from experience, reading and the data available. Uganda is bounded on the north by the Sudan, on the west by Belgian Congo, on the south by

Tanganyika and on the east by Kenya. Kenya blames Uganda for all cataclysmic happenings except drought and earthquakes. Uganda is an upland country with a snow-covered mountain Ruwenzori (16 794 ft) descending to L. Albert (10 030 ft) contains the lakes Victoria, Edward and Albert and the Albert and Victoria Nile rivers. Two excellent maps accompany the report.

The author's work on plague, plague rodents and plague fleas may truthfully be set down as pioneer investigation, for the previous surveys of Uganda had reference to tsetse-fly disease and sleeping sickness. Many of the early data are erroneous and cerebral meningitis has been mixed up with plague in African diagnosis. His deductions lead him to the view that plague has existed in Uganda from ancient times, perhaps since 549 B.C., smouldering, latent but never absent. This view of the antiquity of plague in a country though not autochthonous reminds one of the existence of plague in India before the arrival of pandemic plague from Hong Kong to reinforce a negligible mouldering rat enzootic. The subject is well treated by Hanlon and was specially investigated in the Humayun Hills by Walton and Stewart Douglas of the Royal Indian Plague Commission of 1888. But to return to Uganda. There is no sylvatic plague in Uganda and the author throws out a warning that a field rodent dead of apparent plague must be certified as a death due to *P. pestis* and not some other *Pasteurella*, also that it is a vector not a victim, of plague. Two invasions are mentioned of Uganda, one of the mammalian vector *Rattus* *s. albus* replacing (1801-1806) an equally good plague vector *Rattus* (*mushroom*) *couchei* *malabar* and of *Xenopsylla cheopis*. The flea invasion however seems to have been earlier and to some extent independent of its chief host *Rattus albus*. Nevertheless it is not *X. cheopis* that is the prime plague flea of Uganda, but *X. brasiliensis* which is given as the normal initiator of all plague outbreaks in Uganda and in many areas in Kenya. *Xenopsylla laeviceps* a close relation, was presumably the predecessor of *X. cheopis*.

To conclude when plague occurs in Uganda at the present day four factors are invariably present these being (1) presence of *Rattus* *s. albus* (or in the past *R. couchei*) (2) presence of a sufficiently large population of *Xenopsylla brasiliensis* or *X. cheopis* (3) presence of *Pasteurella pestis* and (4) an average rainfall not below about 45 inches. For an epidemic to occur a fifth factor intimate contact between rats and man is required. A distinction is to be drawn between "huts" and permanent buildings and between corrugated iron roofs and thatch as regards rat infestation. The invading rat *Rattus albus* which is not a burrower and prefers to nest in thatch still finds ample opportunity to nest in the hut with a kerosene-tin or iron roof or in burrows already prepared by *R. couchei*.  
H. F. Harvey

HUANG, C. H. HUANG C. Y. CHU L. W. & HUANG T. F. Pneumonic Plague. A Report of Recovery in a Proved Case and a Note on Sulfadiazine Prophylaxis. Amer. J. Trop. Med. 1948 May, v. 28, No. 3, 361-71, 3 figs. (30 refs.)

Reports of recovery from pneumonic plague are becoming frequent and, if not recovered, unusual prolongation of life. Five of the cases are uncomplicated as regards therapy. The salient points in the present case are these:

A case of pneumonic plague proved morphologically, culturally and experimentally, presumably contracted in the laboratory by man (33), at commencement of symptoms Feb. 11, 1947, subacute (fever to Mar. 3 but resolution delayed) up and around June. May 7 sputum bloody, sometimes red, sometimes of tomato-sauce tint, complication of malaria on Mar. 17 due to blood transfusion, sulfadiazine was started within 48 hours and amounted to a total of 87 gm. between Feb. 13 and Mar. 3 when it was

stopped, because the white cell count had dropped to 3,200/cmm, streptomycin therapy about 72 hours after onset, of which the first intramuscular injection was 100,000 units with similar rather small doses every 3 hours. The dose was later increased to 2-3 million units a day, between Feb 22 and Mar 4 about one million units of penicillin were also given for secondary infections, during treatment 2 blood transfusions, 2 plasma transfusions and 6 intravenous infusions of 5 per cent glucose were given, oxygen inhalation was given as required and 10.2 gm quinine sulphate for malaria, the plague bacillus isolated on Feb 14 was sensitive to both streptomycin and sulphadiazine, that of Feb 26 was resistant to streptomycin, but sensitive to sulphadiazine, the patient had had 2 injections of Haffkine Institute plague vaccine in 1942 and another in China in Dec 1943.

Contacts, 3 of them close, and 15 in all, none of whom had been prophylactically vaccinated, received 3 to 6 gm sulphadiazine daily for adults and proportional doses to children, for one week by the mouth. None of them developed the disease.

One of the conclusions drawn is that sulphadiazine and streptomycin may be more efficacious when used in synergistic combination.

W F Harvey

MEYER, K F, QUAN, S F & LARSON, A. Prophylactic Immunization and Specific Therapy of Experimental Pneumonic Plague. *Amer Rev Tuberculosis* 1948, Apr, v 57, No 4, 312-21, 1 fig & 5 charts

In this short article the authors present experimental methods, histological confirmation and sharp conclusions, which should attract the attention of workers in other organismal infections than plague, where animals are also susceptible with man. The therapy is both prophylactic and curative.

No evidence exists that there is a variety of *P. pestis* which is pneumotropic, and the bacteria isolated from bubonic and pneumonic plague are identical. The animals used in these experiments were guineapigs and mice, which are in some respects contrasted animals in their reactions to the plague bacillus, or rather to the plague toxin. A survival rate of only 21 to 25 per cent in mice after intranasal infection is contrasted with a rate of 80 per cent in guineapigs, the inequality being attributed in part at least to differences of susceptibility to plague toxin. A careful histological examination, so rare in well-established bacterial diseases shows the course of the infection after intranasal instillation of highly virulent plague bacilli in animals anaesthetized with barbiturate ("4 to 8 000 organisms per 0.05 cc per mouse and 0.3 cc for guineapigs") — In 5 to 10 minutes one-tenth of the administered bacilli have reached the deeper respiratory passages. Rapid increase of the bacilli is demonstrable in the lungs, so that by the 48th hour 20 to 500 million "may be cultured from the entire mouse lung. At this stage the blood stream is invaded. Guineapigs as a rule are not visibly ill for the first two days but die suddenly between the third and fifth day."

The conclusions will fully reveal the importance of this work. — (1) Intranasal instillation of highly virulent plague bacilli produces in mice, guineapigs and cotton rats a primary pneumonia which is anatomically indistinguishable from that observed in man. (2) Active immunization with avirulent strains of *P. pestis* or chemically killed plague bacilli in the form of particulate antigens confers on mice a definite and on guineapigs a marked protection against an intranasal challenge infection. (3) Concentrated antip plague rabbit sera possess prophylactic and to a slight degree curative values in pneumonic plague. (4) Sulphonamides are not very effective, though "when combined with antip plague serum, their therapeutic value, definite in bubonic plague, is

equally demonstrable in the pneumonic type. (5) Streptomycin is thus far the most effective therapeutic agent known for the treatment of plague infections, both bubonic and pneumonic. Over 80 per cent. of experimentally infected mice when in the septicaemic state of lobular plague pneumonia, may be cured with 5 mg. of streptomycin. It is recommended that human pneumonic plague be treated early in the course of infection with daily doses of 4 to 6 g. of streptomycin and that treatment should continue for not less than six to ten days."

W. F. Harvey

BARNETT S. A. Rat Control in a Plague Outbreak in Malta. *J. Hyg.* 1948 Mar v 46 No. 1 10-18, 1 map, 2 text figs. & 4 figs. on 2 pls [17 refs.]

A straightforward clear account is given by the author of an anti rat campaign in Malta. The rat is the agent in development of plague and the flea-borne endemic murine typhus in the island. In Malta the rat problem was that of a densely populated subtropical area but not wholly urban for the country is intensively cultivated. Human plague had made its appearance on June 17. Altogether in the course of a year since when there have been no further human infections, there were 80 cases with 22 deaths. During this year 22,907 rats were examined, 659 being *R. rattus*. Only 20 rats were diagnosed as plague infected and of these 15 were *R. norvegicus*. It is *R. norvegicus* that is the common rat in Malta and it evidently played an important part in carrying plague. Reliance was placed for reduction of the rat population on poisoning by zinc phosphide arsenious oxide red squill and alphanaphthylthiourea (ANTU). The method was prebaiting, followed by poisoning with baits and poisons of known efficacy and change of both bait and poison for follow-up treatments.

W. F. Harvey

## CHOLERA

IN DER BECK, M. Die Epidemiologie der Cholera in Frankreich. [The Epidemiology of Cholera in France.] *Zuckerf. Hyg. u. Infektionskrankh.* 1948, Apr 1 v 127 Nos. 8 & 9, 526-34

A historical study

WAMID, L. L. A Short Note on Contacts of Cholera at Embaba Fever Hospital. *J. Hyg. Egyptian Med. Ass.* 1948 June 31 No. 6 487 &

The author examined from one to three or more wabs each from 600 contacts of cholera during the epidemic of 1947. Post mortem studies were found in 16 persons without symptoms and it is stated that 17 of these were carriers for only two days. The longest duration of the carrier state found was 7 days. Only 3 of the contacts showed evidence of the disease. A dramatic effect of sulphonamide prophylaxis on the carrier state was observed, notwithstanding the fact that to be related to cholera vaccination or its absence. Two wabs showed latent period of 5 and 6 days with no symptoms between the incubation and the beginning of the carrier state. (This paper is so much brief further details of these findings would be desirable.)

W. J. O'D. Burckhardt

HARVEY W. Differential Diagnosis of Cholera. *J. Hyg. Egyptian Med. Ass.* 1948 June v 31 No. 6 41 &

Two wabs are the first and the last will show the same type of each of the three clinical forms the cholera. The text books, which is selected true

vibrio These are "Differentiation of cholera from the clinical point of view is a rather difficult problem" and "Every case of diarrhoea without vomiting should be provisionally suspected as cholera and isolated in the hospital, where the final diagnosis of cholera is either proved or disproved"

Notes on examples of diseases which are mistaken for cholera and which were met with in the hospital at Abbassia form the subject matter of the article. These were (1) food poisoning (2) acute metallic poisoning, (a) the most important, arsenical poisoning, (b) acute mercurial poisoning by mercury chloride taken suicidally (3) severe types of dysenteries, (a) bacillary dysentery, (b) amoebic dysentery, (c) malarial dysentery, (d) bilharzial dysentery, (e) ciliate dysentery. [There is no mention of vibrio dysentery, El Tor dysentery, so that presumably it was not met with, or was included with true cholera.] (4) pellagra (5) tuberculous enteritis (6) some mild forms of diarrhoea post-prandial, nervous, gastrogenous or an intestinal carbohydrate dyspepsia (7) acute appendicitis (8) Addisonian crises (9) Graves's disease (10) summer diarrhoea, "cholera infantum" (11) some others. The author draws attention to uraemia, a terminal feature of cholera, to remark that "uraemia itself due to kidney disease or other factors gives rise to diarrhoea, vomiting, dehydration, and acidosis—a picture very similar to cholera"

W F Harvey

BALIGH, A. Complications encountered among Cholera Cases treated in Ismailia Isolation Camp. *J Roy Egyptian Med Ass* 1948, June, v 31, No 6, 468-70

The commonest complication of cholera encountered by the author was *heart failure*. This occurred in (1) most of those patients dying within 24 hours of admission as a result of sudden changes in the blood and ischaemia, (2) sometimes during treatment with large transfusions given rapidly, (2) occasionally during apparent convalescence as a result of toxæmia and myocarditis. Extra-systoles were quite common at this stage, but corrected equilibrium of the blood soon caused them to disappear. Electrocardiographic examinations confirmed that the heart may be so deranged in severe cholera as to fail at any moment during convalescence. In fact 8 apparently well patients did die suddenly at this stage in 10 to 20 days from the onset of the disease.

*Persistent suppression of urine and uraemia* caused many of the early deaths before lines of treatment were completely established. It was usually due to dehydration and retention of nitrogenous products.

*Abortion and premature labour* were constant in those pregnant women who had cholera. Of 7 such, 4 aborted, 2 had premature labour and 1 died during labour at term. All of them died within 2 to 3 days, except 1 who died of pneumonia in 5 days. These abortions were complete and without haemorrhage and were attributed to severe purgation, severe reflex uterine contractions and toxæmia. The author does not recommend any interference in such cases, as the abortions were always completed quickly without it.

Five patients died of *pneumonia* and 2 from *pulmonary oedema*, both of the latter suffered from suppression of urine, but the author adds that "oedema was due to sudden overhydration with saline solution". During the recovery stage, 3 patients developed *maniacal conditions*, 1 recovered completely and the other two died.

*Parotitis and paraplegia* each occurred once and cure was complete in each case.

[The statistical value of this note would have been enhanced by a statement of the total number of cases seen.]

H J O'D Burke-Gaffney

LAMTRI S. C. Sulphadiazine and Sulphaguanidine in Cholera. *Indian Med Gaz.* 1948 Jan., 83, No. 1 74-8.

Most of the work on the value of sulphonamides in cholera has gone to show the superior value of sulphaguanidine over the other forms as being non-absorbable and non-toxic. In this study the author uses sulphadiazine less toxic than sulphathiazole. In the initial dose of 2 gm. followed by 1 gm. 4 times a day as a comparison with sulphaguanidine. Of course in cholera symptomatic treatment is always required to combat dehydration demineralization and depletion of colloids. Altogether 139 patients received sulphadiazine 111 sulphaguanidine and 43 got calomel. The result is interesting. Both sulphaguanidine and sulphadiazine are beneficial in cholera. If children and old men are excluded the death rate for the intermediate age group, the majority group, is practically the same with both drugs—8.68 per cent. with sulphadiazine and 8.49 per cent. with sulphaguanidine. W. F. Harvey

GOHAR, M. A. & ISA, A. A. Cholera Vaccines. *J Trop Med. & Hyg.* 1948 July v 51 No. 7 144-7

Gohar has seized the opportunity of the cholera epidemic in Egypt to make useful animal experimentation on vaccines, using the horria strain itself for this purpose. The animals used were rats and the LD<sub>50</sub> intraperitoneal dose of the horria cholera vibrio was 4 000 million organisms. His five vaccines, for each of which 25 rats were provided were: (1) Heat killed phenol-preserved suspension, at 4 000 million/ml. of which the lethal dose subcutaneously was 4 ml. (2) Formalin-killed phenol preserved suspension, of the same strength and having the same lethality as the first. (3) Soluble extract obtained by adding an equal quantity of normal sodium hydroxide to a suspension at 8 000 million/ml. incubating at 37°C for a few hours until clear and neutralizing with HCl to pH 7.5. The lethal subcutaneous dose was 3.5 ml. (4) Toxoid obtained by treating the No. 3 toxin with 0.7 per cent. formalin and incubating at 37°C for 70 days, by which time it had become non-toxic and the animals immunized with it could resist big doses of toxin. (5) A mixture in equal parts of vaccine and toxoid.

Also, three batches of rats were used the 8th being the control untreated batch. The test dose the LD<sub>50</sub> and the immunizing dosage 2,000 and 4,000 million organisms or equivalent subcutaneously 1 week interval. The survivals of the 6 batches in the order given were 16 17 15 14 21 and 11 or in percentages, 64 68 60 58 84 44. It must be admitted that the number of animals used is too small and the results obtained can only be looked upon as suggestive in favour of the mixture containing equal parts of both toxoid and vaccine.

An important remark made by the author while commenting doubtfully on the distinction between haemolysation and haemolysis by slants may be recorded. We found when cultures of the horria vibrio were kept in the incubator for three days that the clearing was just as intense as that produced by the truly haemolytic El Tor brew. This shows that the difference between the two organisms is more of quantitative than a qualitative nature.

The toxoid vaccine mixture takes long time by complicated procedure to prepare and the author describe a simple method of preparing an alum precipitated cholera vaccine mixture. See this Bulletin 1948 45 601.

W. F. Harvey

# AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

- SHAFER, J G, RYDEN, F W & FRYE, W W Studies on the Growth Requirements of *Entamoeba histolytica* III The Growth and Multiplication of Two Strains of *E. histolytica* in a Transparent Medium without the Addition of Rice Flour or other Particulate Matter and without Demonstrable Bacterial Growth *Amer J Hyg* 1948, May, v 47, No 3, 345-50

The culture of *Entamoeba histolytica* in the absence of bacteria has been attempted for a long time, and these workers have progressed a further step towards the goal. They used a medium consisting of (a) the supernatant fluid from a culture of a streptobacillus [this *Bulletin*, 1948, v 45, 786, 787] in a thio glycollate rice flour medium, (b) a bacteria-free filtrate of the specific bacteria complex grown in egg-slope-buffered-saline medium, (c) normal horse serum, and (d) a low concentration of penicillin. Amoebae obtained from fresh specimens could not be grown directly in this medium, they first had to be passed through media containing higher amounts of antibiotics. The culture must be anaerobic and subcultures should be performed every 48 hours (at 37.5°C). The few streptobacilli present in the cultures either fail to multiply or die out—even after 14 days the medium remains clean. P C C Garnham

- STEWART, G T & JONES, W R The Pathology of an Experimental Amoebic Infection in the Rat *Ann Trop Med & Parasit* 1948, Apr, v 42, No 1, 33-45, 5 text figs & 2 pls [36 refs]

By the technique described by JONES [this *Bulletin*, 1947, v 44, 313] rats were inoculated intracaeally with *E. histolytica*. In different groups, 67-90 per cent of the animals became infected. The inoculum was 0.2 cc of the mixed centrifuged deposit of amoebic culture with an equal volume of 10 per cent gastric mucin. For the study of bacterial action, broth cultures of bacteria were added to the inoculum or were given orally before or after establishment of the amoebic infection. Heavy doses of bacteria ranging from 10 to 1,000 million organisms were administered. In certain experiments, phthalyl sulphathiazole (500 mgm/kgm orally) or penicillin (500 units subcutaneously) was given four times in the 48-54 hours before or after the operation. After periods ranging from 1 to 14 days the animals were killed and the caeca examined. The infection was judged by the numbers 5 to 0, according to the degree of infection. Heavy infection, ulceration, numerous amoebae, 5, inflammation and mucus numerous amoebae, 4, inflammation, many amoebae, 3, normal, many amoebae, 2, normal, few amoebae, 1, normal, no amoebae, 0. For two strains of *E. histolytica* the infectivity and virulence were definitely related, but one strain gave a high percentage of virulent infections unrelated to the infectivity.

The mucosa of the caecum showed evidence of invasion within 24 hours in the shape of minute erosions of the columnar epithelium. Later there was invasion of the villi and crypts by amoebae with some necrosis of the adjacent mucosa. At a later stage the mucosa at the edge of the lesion became heaped up and formed a follicular ulcer containing mucus and amoebae. Beyond the ulcer the mucosa remained healthy. In another type of lesion there was widespread cellular infiltration by polymorphonuclear leucocytes of the tissues around the original break in the mucosa. There was congestion and focal lymphoid hyperplasia. Amoebae were often scanty. Lesions of this type were especially prevalent when virulent bacteria had been administered in the inoculum. Between these two types of lesion many intermediate forms occurred. At a later stage (3-7 days) the caecum was grossly ulcerated and thickened with

a copious exudation of mucus into the lumen and local peritonitis leading to adhesions. Amoebae were found chiefly in the bases of the ulcers or in the loose exudate sometimes forming a solid mass. Isolated amoebae were seen in the submucosa and rarely outside the muscularis mucosae. Healing would begin at any time but usually commenced after seven days. In some cases this was retarded for a few weeks. Death sometimes occurred after 3-4 days but most fatalities were during the first 24 hours and were associated with coliform bacteraemia. No amoebae were observed in the liver.

The lesions were aggravated by the administration of *Bacterium* and paracolon bacteria. The strain of paracolon remained in the bowel for several days. The administration of penicillin controlled the bacteria and profoundly reduced the severity of the infection. Penicillin was active both prophylactically and therapeutically. Phthalyl sulphathiazole and other sulphonamides were partially effective prophylactically but had no therapeutic effect though given with penicillin they seemed to increase its activity. The result of the work is that young laboratory rats are susceptible to amoebic infection the bacterial flora being the major factor in the pathogenesis. With the bacteria controlled by penicillin minimal lesions are produced. In some of the young rats after the acute infection had subsided, cysts were found in the intestine. In general, the infection resembles that in human beings.

C. M. HENRY

GHOSH, N. N. GHOSH H. & RAY, J. C. A Preliminary Note on Complement-Fixation Reaction in Amoebiasis. *Indian Bioclinic & Exper Med* Calcutta, 1948, Jan. Feb. v 8, Nos. 1/2, 3-10 [21 refs.]

The serological diagnosis of amoebiasis has been re-examined with a view to the preparation of a more satisfactory antigen for the complement deviation test than has previously been devised. An antigen was prepared from cultures of a strain of *E. histolytica* virulent to humans by penning down the amoebae in the supernatant fluid of cultures at 1000 r.p.m. for three minutes. At this speed the major portion of the accompanying bacteria was left in the supernatant fluid, which was discarded. The washed sediment was triturated in sand to a fine paste and diluted in phenolized distilled water (0.4 per cent. phenol) to nine times its volume. After filtration through filter paper it was stored in the ice chest until required for use. The working dilution of this antigen was 1 in 10 and it was employed with a deep-cell haemolytic system. The serum under test was inactivated at 55 C. for half an hour and diluted to 1 in 5 before use. Control bacterial antigen were also prepared from the amoeba culture-tube.

The authors found their antigen more potent and specific than those prepared by alcohol extraction methods. Of 14 persons giving a positive complement deviation test 7 proved to have intestinal *E. histolytica* infections and 7 had amoebic liver abscesses. Of 46 persons giving a negative test 2 were found to harbour *E. histolytica* both of these were free from symptoms of the infection. The table setting out these results is somewhat difficult to follow.

J. K. D. ILM

STEWART, G. I. O'MEARA, P. J. & KIRKHAM, W. L. Observations on Amoebiasis in Ceylon. *J. Roy. Soc. Med.* 1948 Jan. 34 v 1, 1-7 [2 refs.]

The authors describe in detail the beginning of the disease with fall in the count of eosinophils, the onset of diarrhoea and the development of a fatal outcome. The authors state that the disease is not fatal in any case at two years of age during the war.



Faeces of Asiatic cooks and stewards in three establishments in the different climatic zones of Ceylon were examined by the copper sulphate flotation method. In the low country it was 9 per cent, at Diyatalawa, up country, 13 per cent, and in Trincomalee, low country dry zone, 11 per cent. It is to be noted that the percentage of incidence when four specimens were examined was approximately twice as great as when only one was examined. The influence of such a carrier state on the incidence of fresh infections in Europeans exposed to contagion is given in a table which purports to show that the incidence of fresh cases progressively diminished as the food-handlers were effectively supervised. In the majority of instances it seemed likely that constant exposure to infection first occurred in the mess. After a survey in December, 1944, three cooks and eight stewards were found infected with *E. histolytica* and were either treated or transferred to other duties. Thereafter infected food handlers were excluded and this was associated with an abrupt decline of fresh cases. Other means of acquiring infection were eliminated as far as possible. No uncooked fresh vegetables were served and flies were not abundant. A similar fall of incidence occurred in Trincomalee in June 1946 after similar measures had been taken.

Admissions for bacillary dysentery at some periods exceeded those for amoebiasis, and in some a sharp attack of bacillary infection appeared to unmask a latent amoebic infection. But bacillary dysentery rarely caused permanent injury. In this respect amoebiasis was in contrast. Severe cases, complications and relapses were comparatively common and about a quarter relapsed within a few months. The danger of reinfection was high. There were no fatalities among Europeans, but general impairment of health was a serious problem.

The slow onset is shown by a table which indicates that 68 per cent had been in the station more than six months before the onset of symptoms. The remaining 32 per cent seem to indicate that signs of infection may develop in less than six months, but for the most part the patients were in good general condition.

In each case diagnosis was made by faeces examination and in a few by rectal scrapings.

The main clinical features are tabulated. Diarrhoea occurred in 84 per cent, constipation in 10, abdominal discomfort in 81 and tenderness in 59, blood in stools in 49, vomiting in 18 and nausea in 16, loss of weight in 11, pyrexia in 14 and lassitude in 16.

As regards diarrhoea there was a loose precipitate morning stool, but as such an occurrence is frequent in normal individuals, the best pointer for diagnosis seems to lie in recurrent diarrhoea or alteration of the bowel habit.

Sixty-seven cases were dysenteric, but the remainder (73) were diagnosed as amoebiasis from the presence of *E. histolytica* cysts in the faeces.

Severe cachexia and signs of nutritional deficiency were rare and occurred only in patients with relatively long histories of illness.

Plasma protein estimations were performed upon a random sample of 26 patients of which six showed significant degrees of hypoproteinaemia, each being a severe relapsing case. Lowering of plasma proteins in certain cases has been adduced as evidence of nutritional deficiency in amoebiasis, but it is possible that hypoproteinaemia may be a manifestation of liver damage. Pyrexia was mild and lasted only 24 hours. When persistent and high it was associated with definite signs of hepatitis and once with massive typhlitis.

*Sigmoidoscopy*—The classical lesions are not in dispute, but some of the early changes are still ill defined. Pin-point craters, patchy hyperaemia and localized oedema were observed in cyst passers—changes which were best seen with a snuffing eye-piece.

Raised pin-point yellowish dots with an inflammatory areola were often seen at the recto-sigmoid junction. These scrapings usually yielded vegetative amoebae but occasionally mucoid material with a few macrophages and leucocytes. A day or two later stool examination or sigmoidoscopic scraping, revealed *E. histolytica*.

Six cases of amoebic hepatitis were seen during the period of review. Haemorrhoids and pruritus ani were not uncommon but the most troublesome complication was post-dysenteric colitis. Apart from *Shigella* infections (bacillary dysentery) the nature of secondary infection still awaits definition. In their experience this occurs only in late and relapsing cases but clinical evidence is obtained only when the exudate becomes purulent. As regards treatment no original methods are claimed. Emetine injections were given during the dysenteric phase or where hepatitis was suspected sulphonamides, occasionally with penicillin, where the appearance of frank pus in the stools suggested the presence of heavy secondary infection. EBI quinorol and stovarsol were given for the remainder of the course.

Criteria of cure were Twelve negative stools for *E. histolytica* and exudate sigmoidoscopy, no active lesions, not more than three bowel movements per day.

The relapse rate between dysenteric and non-dysenteric cases was remarkably similar which suggests that a patient with dysentery has as good a chance of cure as one passing cysts.

The custom of giving ten or twelve injections of emetine to every case has been to a great extent abandoned, but the authors, on the supposition that vegetative amoebae in lesions of the upper colon become transformed into cysts in the lower colon, suggest that there may be good reason for its continuance in patients without dysenteric symptoms. [See also this *Bulletin* 1948, v 43, 357 1947 v 44 818.] P. M. W. B. B.

HULLASHO, A. L. Amoebiasis hepatis. [Liver Amoebiasis.] *Am. J. Trop. Med. Hyg.* 1948, July 1 v 92 (supp. No. 3), 2214-20.

PARMER, L. G. On the Relative Efficacy of Emetine in Intestinal and Hepatic Amoebiasis. *P. & Soc. E. Afr. Biol. & Med.* 1948, June v 68, No. 2, 362-3.

It is well known that while emetine is effective in amoebic hepatitis and early amoebic abscesses, it is ineffective by itself in amoebic dysentery. This is usually explained on the grounds that the drug is capable of destroying trophozoites but not cysts of *E. histolytica* and since cysts are not usually found in the tissues outside the intestinal lumen hepatic amoebiasis is more susceptible to emetine treatment. This does not however explain why the drug can eradicate trophozoites in the liver and although emetine has been used in amoebiasis for more than 35 years the full answer is that the tissue distribution and concentration of this alkali has not been reported.

Working in the Pharmacology Section, Research and Clinical School, Army Medical Centre, Washington D.C. the author injected 1 albino rabbit (5 kgm. weight) intramuscularly with 8 mgm. kgm. emetine hydrochloride in aqueous solution. The rabbit was sacrificed in groups of 3 at intervals of 1 hour to 28 days. The excreta were analysed for emetine by a method adapted from that of B. A. C. DE VRIES and DINK [this *Bulletin* 1947 v 44 90].

The results for 28 days are shown in table which indicates that within an hour the concentration of emetine in the liver was 4.9 mgm. kgm. compared with 5.5 in the intestine. At 1 hour the figures were 41.6 and 1.7 respectively.

and in 4 days 15.4 and 1.2 mgm./kgm. Thereafter the drug continued to be found in the liver in decreasing quantities up to the 28th day, while none was detected in the intestine from the 5th day onwards.

The finding of a high concentration and prolonged presence of emetine in the liver, compared with low concentration and transient presence in the intestine, is put forward as the explanation for the efficacy of the drug in hepatic amoebiasis and its failure in amoebic dysentery in man. [While one hesitates to argue from animal to man in experiments of this nature, the highly significant results of these experiments and their possible implications demand further and extended investigations on this important point.]

H. J. O'D. Burke-Gaffney

DWORK, K. G. The Use of Para-Aminobenzoic Acid in Amebiasis. Preliminary Report. *Bull. New York Acad. Med.* 1948, June, v. 24, No. 6, 391-3.

This study was conducted in the Department of Health, New York City, on 12 out-patients with *E. histolytica* infections, all but one of whom were Porto Rican emigrants. As the drug, which is rapidly excreted, was not given at night and no blood levels were done, it was believed that if encouraging results followed, even more favourable results might be expected under hospital conditions. The drug used was the sodium salt of paraaminobenzoic acid (sodium paba).

The dosage of sodium paba employed is not stated in the text, but in a table listing individual results, sodium paba treatment is shown as varying from "2.0 q3h 7 days" to "2.0 q2h 14 days" which presumably means 2 gm. every 3 hours for 7 days to 2 gm. every 2 hours for 14 days.

Nine patients completed the course and four of them had negative stools after 4 to 30 weeks. Of seven patients with symptoms, six showed improvement or disappearance of symptoms after treatment.

It is noted that the non-Porto Rican case had been refractory to carbarsone therapy but cleared up with sodium paba.

Another table shows that the successes were obtained in four of the five patients who received the drug at intervals of 2 hours, and that of the five failures four occurred in those treated at intervals of 3 or 4 hours [see also BRACKETT and BLIZNICK, this *Bulletin*, 1948, v. 45, 80].

H. J. O'D. Burke-Gaffney

YOUNG, Viola M. & FELSENFELD, O. The Occurrence of Intestinal Protozoa in Adults in San Juan, Puerto Rico. *J. Parasitology* 1948, June, v. 34, No. 3, 229-30.

The authors refer to previous surveys of intestinal protozoa in Porto Rico by POINDEXTER [this *Bulletin*, 1934, v. 31, 281], FAUST *et al.* (*Puerto Rico J. Pub. Health & Trop. Med.*, 1933, v. 9, 447), and ACOSTA MATIENZO (*ibid.* 1946, v. 21, 369). The difference in scope and methods of these surveys is pointed out and the authors then describe the present survey designed to ascertain the existing endemicity of intestinal protozoal infections in San Juan and suburbs.

They obtained fresh stools from 600 adult patients, without diarrhoea, in the Presbyterian Hospital of San Juan. The patients in this hospital represented all ages and classes of the general population, but no children were included in this survey. The stools were examined by direct smear and by zinc flotation (Faust).

The results are shown in a table and compared with those of the previous three surveys. It is pointed out that ACOSTA MATIENZO considered her percentages too low as she only used direct smear. This is reflected in the present survey where protozoa were found more frequently.

*E. histolytica* was found in 17.33 per cent. of persons compared with 1-4 per cent. in Pomdester's survey and 14.3 per cent. in Faust's rural survey 15 years ago. On the other hand, *Giardia intestinalis* (3.83 per cent.) and *Isospora hominis* (1.83) were considerably fewer which may have been due to improved sanitary conditions and to the exclusion of children from the present survey. It was observed that 23.5 per cent. of persons harboured *Endamoeba* sp. compared with 16.3 in Faust's survey, which the authors believe may be due to frequent shifts of population from the Continental United States where this parasite is said to be increasing.

Protozoa were found in 57.16 per cent. of the persons examined—two species were found in 14 per cent., three in 8.5 per cent., and four in 0.5 per cent.

The authors point out that the incidence of *E. histolytica* in symptomatic adults has not receded during recent years from the high rates found by FAUST *et al.* Frank clinical amoebiasis is rarely found in the San Juan area, but the present findings indicate that the danger of it persists in Puerto Rico. [The date of the paper by FAUST *et al.* is incorrectly given in the list of references as 1943.]

H. J. O'D. Burke-Gaffney

LEIS, CARL E. *Giardiasis intestinalis y síndrome convulsivo* [Intestinal Giardiasis and the Convulsive Syndrome.] *Revista Méd. y Quím.*, 1948, June 4 v. 25 No. 23, 1034-7.

An account of a case and discussion.

GLAUBER, W. *Massive Infektion mit Isospora hominis s. Del.* [Massive Infection with *Isospora hominis*.] *Med. Klin.*, 1948, Jan., v. 43 No. 1—23.

This note concerns a refugee from Sudetenland who was admitted in August 1946 in a comatose condition. His illness had started suddenly a week before with profuse watery diarrhoea. He was erythematous and the condition suggested a diagnosis of typhoid. General and laboratory examinations, including agglutination, did not provide a diagnosis but microscopic examination of the stools showed masses of coccidia of the type *Isospora hominis* (see p. 100). In a single microscopic field with the oil immersion lens, 51-6 coccidia were seen. A brief description of the parasites is given. The condition resisted sulphonamide therapy but apparently responded to treatment with Rivanollettes—2 tablets 3 times daily [1 tablet contains 0.025 gm. of Rivanollet for a week. After 2 days the stools were formed and after 4 the coccidia were no longer detectable in them. Fourteen days after the course of treatment the patient had put on 10 lb. in weight. He has been followed up for a year—no relapses have occurred and he is fit for work.

The author discusses the differential diagnosis of acute diarrhoea of this nature and refers to the uncertain pathology of coccidiosis. It should be kept in mind when one is dealing with sulphonamide resistant diarrhoeas, the prompt response to Rivanollettes in this case was remarkable. This claim of a severe condition attributed to infection by *Isospora hominis* and its dramatic cure is worthy of more detailed evidence in support of it.

H. J. O'D. Burke-Gaffney

LAMY, L., MARCHEL, G. & CHEVRIER, A. M. *Notes sur le diptère et son Entomomus parasite de l'intestin de l'homme*. Further Notes on an Entomomus Parasite in the Human Intestine. *Bull. Soc. Path. Exot.* 1948, 41 No. 34 154-8, 1948.

Under the name *Entomomus* Lamy *et al.* propose the authors describe a flagellate which was grown in culture from the faeces of three colonial officers who

## Leprosy

suffered from diarrhoea. The flagellate was globular and measured on an average  $7\ \mu$  in diameter. There was a large nucleus and three long flagella arising from a point near the nucleus. In addition, in the majority of flagellates, a club-shaped process  $4\ \mu$  in length arose from the body. The flagellate was not found on microscopic examination of the faeces and the authors conclude that it must have been present in the encysted stage which was responsible for the growth in culture. They discuss the nomenclature of the organism and place it in FONSECA's genus *Enteromonas*, though he gave no account of the club-shaped process. Because of the process they place it in a new species as *E. hervei*, but it seems probable that the presence of the process would justify a different genus from *Enteromonas*.  
C M Wenyon

## LEPROSY

McCoy, G W *Leprosy in California—Danger of Infection* Pub Health Rep Wash 1948, May 28, v 63, No 22, 705-12

This is a careful study of the conditions under which leprosy infections occur in the mildly endemic area of California, with an incidence only exceeded in the United States by the defined endemic areas of Louisiana, Florida and Texas. Among 475 cases up to 1940 not more than 14 appear to have been infected in California itself. The main sources of imported infection were, first, China and other Far Eastern countries, and second, the neighbouring endemic areas of Mexico and Louisiana, a very large majority being males. The present inquiry deals for the first time with probable infections within the State, by studying the data accumulated by the health department and the Louisiana state leprosarium. The data were collected by interviewing the patients, three family group infections were found among those who had lived in California all their lives, seven out of eight of whom had lived with leprosy parents, three were examples of conjugal infections. Among approximately 500 cases inquired into, only 23 appear to have been infected in California itself, this places the State on a level with Minnesota as a mildly endemic area. It also appears that 8 of the infections occurred in a small area in the middle of the State, 6 of them were in children infected by their parents, apart from which the likelihood of infection in the area is very small.  
L Rogers

BRAGA, R V Contribuição ao estudo da lepra no meio proletário da cidade do Rio de Janeiro [*Leprosy among the Poorer Classes in Rio de Janeiro*] *Rev Argentina Dermatofilologia* 1947, July-Dec, v 31, Nos 3/4, 486-92, 7 graphs

During a period of years (August 1939-47), 66,764 industrial workers were examined in Rio de Janeiro, 3,006 were suffering from dermatosis of some kind and 231 were infected with leprosy, i.e. 0.35 per cent of the total and 7 per cent of those with skin lesions. By a series of graphs other details are indicated. The greatest number in any one year was 39 in 1944 and the smallest 20 in 1941, the average being 29 *per annum*. As regards the clinical forms, 93 were of the nerve type, 40 lepromatous and 98 mixed, 196 of the total were males, 35 were females [but as the respective totals are not given, this has little if any meaning, all that is stated is "the number of male operatives was greater"], 185 were Brazilians, chiefly from Rio, Minas Gerais and São Paulo, 38 Portuguese, and 8 of other nations. Those engaged in work liable to be associated with trauma were the most attacked—stone-masons, metal workers and mechanics.  
H Harold Scott

BECHTOLD L. M. Da conveniência de se fazer a lepromina-reação nos funcionários que trabalham em contacto direto com o doente da lepra. [Importance of subjecting Attendants on Lepers to the Lepromin Reaction.] *Rev. I. ginec. Dermatol. fsiologia*, 1947 July Dec. v 31 Nos. 34 484-5.

The prognostic value of the lepromin reaction is well known to leprologists. If lepromatous are negative and the tuberculoid positive in the majority of cases and RORTZAG has reported that reactivation of lepromata is common among the lepromin-negative and that positive reactors do not acquire the disease or if they do the evolution is that of the tuberculoid type. Hence the author proposes that the test should be carried out on all who are about to work in direct contact with leprosy patients. Even those who give no history of contact with patients may give a delayed positive. Those working in leprosaria who react positively may continue in their work, but should be watched so that if they become negative, they may change their occupation and be entitled to favourable consideration of a request for compensation. Observations tend to show that it is rare for healthy officials to contract the disease: seven who have shown symptoms had been in contact with lepers before entering on their duties and one only gave no such history. But though the number may be small, there is no doubt that the possible danger exists and it would be foolish to neglect precautionary measures. *H. Harold Scott*

OLAVO CASTRO V. ALBUQUERQUE, P. B. & DIXARTI, A. V. Reacção, sueroeliza de flocculação na lepra. Su aplicação prática na el diagnóstico da lepra. [The Flocculation Reaction in Leprosy.] *Rev. I. ginec. Dermatol. fsiologia* 1947 July Dec., v 31 Nos. 34 328-31

CASTRO and DIXARTI in 1945 recorded some results with sera of leprosy patients and an antigen with lepromata (see this *Bull.* 1946 43, 849-850, where details of the antigen preparation are given). The authors now report the result of the test in a large number of cases, 1,810, of whom 221 were patients (from 1 group (162 the lepromatous form, 6 the tuberculoid) and 1,589 with healthy subjects (1,108) or suffering from other diseases (syphilis, pulmonary tuberculosis, parasitic infections (malaria, American trypanosomiasis, leishmaniasis), brucellosis, typhoid, etc.) and 104 contact of leprosy. Of the 221 of the lepromatous group 119 (53.5 per cent) gave a positive flocculation, only 3 of 62 (4.8 per cent) of the tuberculoid type, but that 12 out of 224 (5.4 per cent). Of the 1,108 healthy subjects reacted with 15 of the 104 contact 4 (3.7) were positive. Only 10 of the 1,589 healthy and other disease patients gave flocculation. Of these 4 as stated, were living with leprosy patient 3 gave erythronal positive 1 had tuberculosis caecum in the lungs and died soon afterwards, only 1 was clinically healthy. *H. Harold Scott*

HOPEWELL, W. Lactogelification e lepra. (Lactogelification and Leprosy) *Bull. Inst. Hyg. Maroc* 1946, 6 419-21

SCHULMAN S. Influencia benéfica de la reacción leprosa en la evolución de los casos lepromatosos. Good Effect of the Leprous Reaction in the Evolution of Lepromatous Cases. *Rev. I. ginec. Dermatol. fsiologia* 1947 July Dec. 31 Nos. 34 463-64. English summary.

Ten years ago Dr. de Sousa Lima told the author that leprosy patients seemed to be followed by improvement. Lepromatous patient and that in the progress of their disease. The author has now studied this question in 33 patients 2 records, but the cutaneous and visceral the visceral lesions

Speaking of the skin lesions, 12 of the 33 improved and all had had leprous reactions, 7 remained stationary and again all had had the reaction, 14 were worse and of these 4 had had the reaction, 10 had not. Of the 31 with ocular lesions who were studied, 21 had had the reaction and of these in 13 the eye condition had remained stationary and in 8 was worse. Two cases are recorded no such reaction 2 were stationary and 8 were worse. Two cases are recorded in detail illustrating the first of these points, with photographs of the patients showing the changes which took place, both were  $L_2$  cases.

The author's conclusions differ, therefore, from those of BECHELLI and COSTA VALENTE of São Paulo (*Rev Brasileira de Leprologia*, 1937, v 5, Special Number, p 167) who stated that, though some might improve, the majority became worse after the reactions.

H Harold Scott

SCHUJMAN, S & CASTAÑÉ DECOUD, Anibal. Modificaciones histopatológicas comprobadas en casos lepromatosos beneficiados (a) Con tratamiento chaulmoógrico (b) Con tratamiento prominico. (a) Con tratamiento in Lepromatous Patients treated with (a) Chaulmoogra, (b) Promin] *Rev Argentina Dermatofisiologia* 1947, July-Dec, v 31, Nos 3/4, 502-6, 4 figs. English summary.

The authors treated 30 lepromatous patients with chaulmoogra and 10 with promin. From 7 of the former and 2 of the latter biopsy specimens of the skin were taken, one at the start of the treatment, the other later when there was only a residual lesion. Some had biopsies at intermediate stages. The changes are shown by four microphotographic reproductions and the details of the different parts of the skin section in each of the nine are described in a table. These may be summed up by saying that the infiltration of the dermis is much reduced, the corium is thickened owing to reabsorption of the infiltrated area, the bacilli are reduced in numbers and broken up, in some no bacilli can be seen at all. These changes were seen in those treated with either drug, chaulmoogra or promin.

H Harold Scott

FIOL, H, JONQUIERES, E D L, BRUSCO, C M, MELAMED, A J & FIRPO, C J. Tratamiento de la lepra con promin (promamida) [The Treatment of Leprosy with Promin] *Rev Argentina Dermatofisiologia* 1947, July-Dec, v 31, Nos 3/4, 531-7.

The results of treatment by promin of 125 patients suffering with the lepromatous type of leprosy are reported. Forty-three had had less than 6 months' treatment and of these 30 [stated as 69.7 per cent] were improved, 12 remained the same and one was worse, of 71 who had had 6-12 months' treatment 47 (66.2 per cent) were improved and 24 unchanged, none was worse, of 11 who had had more than one year's treatment 10 were better and one unchanged. Tables are given presenting the results in other ways. First, according to total dosage of the drug. Four had received from 900 to 1,300 gm and all had improved, 36 had had 500-900 gm and of these 28 were better, 7 stationary, and one worse, of 85 with less than 500 gm 55 were better and 30 unchanged, none was worse. Another table gives the daily dosage and results. Of 13 receiving up to 1 gm daily 7 were better, 6 stationary, of 59 receiving 1-1.9 gm 35 were better, 10 stationary, 8 received between 3 and 7 gm daily and 7 improved, one remained unchanged. In 106 the Mitsuda reaction was carried out, 6 were marked, 4 weak, and 96 negative.

The results would be still better, say the authors, if chaulmoogra were given at the same time and other adjuvant treatment such as liver, vitamins, general tonics and such like.

H Harold Scott

BECCHINI L. M. Da conveniência de se fazer a lepromina-reação nos funcionários que trabalham em contacto directo com o doente da lepra. [Importance of subjecting Attendants on Lepers to the Lepromin Reaction.] *Rev Argentina Dermatol. filiológia* 1947 July Dec., v 31 Nos. 3 + 484-5.

The prognostic value of the lepromin reaction is well known to leprologists: the lepromatous are negative and the tuberculoid positive in the majority of cases and ROMERO has reported that reactivation of lepromata is common among the lepromin negative and that positive reactors do not acquire the disease or if they do the evolution is that of the tuberculoid type. Hence the author proposes that the test should be carried out on all who are about to work in direct contact with leprosy patients. Even those who give no history of contact with patients may give a delayed positive. Those working in leproseries who react positively may continue in their work, but should be watched so that if they become negative, they may change their occupation and be entitled to favourable consideration of a request for compensation. Observations tend to show that it is rare for healthy officials to contract the disease: seven who have shown symptoms had been in contact with lepers before entering on their duties, and one only gave no such history. But, though the number may be small, there is no doubt that the possible danger exists and it would be foolish to neglect precautionary measures. *|| Harold Scott*

OLMOS CASTRO V. ARCEDE, P. B. & BONATTI, A. L. Reacción, serológica de flocculación en lepra. Su aplicación práctica en el diagnóstico y pronóstico. [The Flocculation Reaction in Leprosy.] *Rev Argentina Dermatol. filiológia* 1947 July Dec., v 31 Nos. 3 + 528-31.

CASTRO and BONATTI in 1945 recorded some results with sera of lepro patients and an antigen with lepromata: see this *Bulletin* 1948 43, 849-850 where details of the antigen preparation are given. The authors now report the result of the test in a larger number of cases: 1,818 of whom 244 were suffering from leprosy (162 the lepromatous form, 82 the tuberculoid) and 1,573 either healthy subjects (1,108) or suffering from other diseases, syphilis, pulmonary tuberculosis, parasitic infections (malaria, American trypanosomiasis, leishmaniasis), brucellosis, typhoid, etc. and 100 contact of leprosy. Of the 162 the lepromatous group 119 (73.5 per cent) gave a positive flocculation, only 3 of 82 (4.9 per cent) of the tuberculoid type: together 122 out of 1,818 (6.7 per cent). Of the 1,088 healthy subjects reacted positively 1 of the 100 contact (3.7) were positive. Only 10 of the 1,573 healthy and other diseases patients gave flocculation. Of these 4 as stated were in contact with leprosy patients: 1 gave very strong Kahn positive, 1 had tuberculous cavities in the lungs and died soon afterwards: only 4 were clinically healthy. *|| Harold Scott*

OPPENHEIM, W. Lactin flocculation in Lepre. [Lactagglutination and Leprosy.] *Ind. Inst. Hyg. Marac.* 1948 6 41-9. (2 ref.)

TRUJMAN, S. Influencia benéfica de la reacción leprosa en la evolución de los casos lepromatosos. Good Effect of the Leprous Reaction in the Evolution of Lepromatous Cases. *Rev Argentina Dermatol. filiológia* 1947 July Dec., v 31 Nos. 3 + 906-12 2 figs. English summary.

TRUJMAN, Dr. de Souza Lima told the author that leprosy reaction seemed to be followed by improvement of lepromatous patients and to retard progress of their disease. The author has now studied this question in patients as regards, first, the cutaneous and second, the ocular lesions.



## HELMINTHIASIS

GAUD, J., FAURÉ & SOLÉ Variations dans le temps des index d'infestation humaine dans la bilharziose vésicale marocaine [Temporary Variations in the Indices of *S. haematobium* Infection in Morocco] *Bull Inst Hyg Maroc* 1946, v 6, 55-60 [10 refs]

Schistosomiasis is usually considered to be an endemic disease, not subject to great fluctuations in incidence, but the authors, as a result of investigations made in Morocco during the period 1940-44, have revised their views in this matter. They quote, for 4 foci of *S. haematobium* infection, the findings of previous investigators, and their own more recent figures, and show that in most of the villages the recent figures are much lower than the earlier figures. In the more recent investigations, moreover, *Bulinus* snails were not easily found. [In one of the tables only the percentages of positive findings are recorded, and in some of the villages the number of persons examined is small, so that the incidence, as calculated must be subject to very large chance of error, nevertheless, the total figures are big enough to justify the opinion that there has been a considerable reduction in incidence.]

They discuss the possible reasons for these differences, which may be as much as 10 to 1 and are usually 3 to 1. Differences in technique are not probable, and treatment cannot account for the change, because in some of the areas it was not given. There may be a seasonal factor, and the examinations were not always made at the same time of the year, but it is unlikely to be important. It seems as if *S. haematobium* infection behaves as an epidemic disease, and that when human infection is comparatively rare the adult infection rate is higher than the childhood rate, and the snails are scanty. The disease is relatively benign in Morocco.

Charles Wilcocks

SCHWETZ, J. Sur l'état sanitaire de la région du Lubilash et tout spécialement sur la bilharziose dans cette région. Rapport sur une reconnaissance effectuée en janvier-février 1946 [Health Conditions in the Region of Lubilash (Belgian Congo), especially as regards Schistosomiasis a Survey made in January-February 1946] *Inst Roy Coloniale Belge Bull des Séances* 1947, v 18, No 2, 519-77, 3 maps & 11 figs on 2 pls

[The river Lubilash lies towards the southern part of the Belgian Congo. In this report the author gives not only the results of examinations of the people carried out by himself and his colleagues, but also the results of work done during the past few years by resident medical auxiliaries who have examined large numbers of people in their own areas. Although *Schistosoma mansoni* is not referred to by name, the whole account is concerned with the results of examinations of faeces, and, no doubt, that is the worm in question. The surveys and examinations here recorded, in spite of the limitations admitted by the author, give an impression of the prevalence of schistosomiasis which could not be so accurately conveyed by figures derived from hospital practice. They show that intestinal schistosomiasis is widespread over the whole area.]

The author remarks that although schistosome eggs are often found in routine examination of the faeces of persons who have no symptoms, it would be unwise to ignore them because the infection can lead to serious and even fatal illness. In 1939 he found that about 50 per cent of the people living on the shores of Lake Albert were infected. In 1945, on his return to the Congo, he learned that the disease was prevalent in the Lubilash area, and was requested to investigate it. In this region there was one medical man (at Katanda), and there were three medical auxiliaries in the countryside. All were working independently of each other. The infection has existed in these parts for at least 15 years,

strict control than the positive and more energetically treated. When the nasal mucus becomes positive the patient should be interned without delay. Great caution should be exercised in releasing interned patients on parole: permission to go about depending on steadily improving clinical condition, disappearance of organisms from the lesions and the possibility of control outside. Tubercloid patients may be kept at home or taken into hospital if necessary, until the nasal smears are negative and the more obvious lesions subside. Lastly, all contacts should have a Mitsuda reaction carried out: those positive should have the privilege of visiting those interned and their friends, while the negative should attend weekly for examination.

H. Harold Scott

BECHELLI, L. M. Posição dos doentes de forma tuberculóide incharacterística (inflammatory simplex) na profilaxia da lepra. [Status of Tubercloid Leprosy Patients in Prophylaxis of the Disease.] *Rev. 4ª seção Dermat. e Sifil. São Paulo*. 1947 July-Dec. 31 No. 3, 4 468-74

This is one of a series of papers presented at the 4th anniversary of the Founding of the Argentine Association of Dermatology and Syphilology. The author pleads for less rigorous treatment of those suffering from the tubercloid or non-characteristic, non-inflammatory, form of leprosy. The prevailing idea among doctors in general and the public is that leprosy is leprosy, and any patient so diagnosed is a menace and should be suspect if not isolated. He shows that this view is unjust to the patient and burdensome to the State and thinks that they should be allowed to go free: live with their families and carry on their occupations (with certain restrictions) under observation but unmolested so long as they remain bacteriologically negative. The actual number of lesions present has no bearing on the case. Naturally, if the condition becomes clinically worse and bacterial examination reveals the presence of *M. leprae* observation should be more strict and examination more frequent. Later improvement may take place and the lesions become free from bacteria, but if the condition continues to deteriorate the patient passes from his former category and segregation and active treatment are called for. In cases under observation the lepromin reaction should be carried out from time to time. Furthermore attention should be paid not only to the patient himself but also to his contacts and associates: though he himself is a burnt-out case or non-infective contacts (family or other) may be positive.

H. Harold Scott

MACDONALD, A. B. Rehabilitation—the Industrial and Social Work of a Leprosy Colony. *Leprosy Review* 1948, Apr. 19 No. 7 45-55

This is an interesting account of 19 years' remarkable work in combating leprosy at Idu in Southern Nigeria, during which an agricultural colony of 3,500 indent patients has been built up with its village hospital, homes, home school, workshop, roads, a canal for transport, agricultural produce, court, market, farms, etc. Medical, educational, industrial, recreational, social and religious work is carried on—all a result of the efforts of Mr Macdonald and his able wife. This article should be read in the original by anyone who has

L. H. T.

C. KINKA & C. DE O. MELO. Infecção de Staphylococcus por um inseto leproso. [Infection of a Rat by a Single Staphylococcal Insect.] *Bol. Inst. L. H. T.* 1948 40 No. 111 421-4

FERRO-LUZZI, G. Studio sulla bilaziosi intestinale da *Schistosoma mansoni* in Eritrea [*Schistosoma mansoni* Infection in Eritrea] Boll Soc Ital di Med e Igiene Trop (Sez Eritrea) 1948, v S, Nos 1/2, 5-18, 2 figs [12 refs] English summary

The first case of infestation by *Schistosoma mansoni* in Eritrea was reported by SATTA in 1934 [this *Bulletin*, 1936, v 33, 553, 953], the second by DIEN in 1935. Now, the disease is endemic in several places in Eritrea, notably in villages around Asmara. Saganetti and Adi Ugri. The author names several of these. Five species of molluscs were identified there, viz *Planorbis abyssinicus*, *P. rupestris*, *Limnaca ruffrayi*, *L. africana* and *Buhus raymondianus*. The first two of these were found naturally infested. Their biological characters, their reaction to temperature, their resistance to drying, etc are noted. Two photographs illustrate a highly infested zone near Szo elot. Children accompany animals to the streams and adults wash and bathe in them and infestation takes place via the skin and by ingestion. Preventive measures follow the usual lines: destruction of vector molluscs, careful supervision of disposal of excreta, education to drive home the ways of infestation, the dangers of infestation of and by water, and, lastly, the treatment of patients.

H Harold Scott

RAPER, A. B. Cerebral Schistosomiasis [Correspondence] East African Med J 1948 June, v 25, No 6 262-3

The author refers to the suggestion made by GELFAND [this *Bulletin*, 1948, v 45 721] that some cases of epilepsy appearing in adult Africans may be due to cerebral schistosomiasis. He quotes the literature to show that the two African species of *Schistosoma* are less inclined to invade the brain than is the Oriental species and in fact the literature of cerebral schistosomiasis appears to indicate that 'up to the present *S. japonicum* holds the field as the sole proved invader of the brain' [for a full discussion of ectopic lesions in schistosomiasis see FAUST this *Bulletin*, 1948, v 45, 716, in his original paper, Faust quotes 56 cerebral lesions, of which 4 are attributed to *S. haematobium* and 8 to *S. mansoni* but only one of these, a *mansoni* infection, was confirmed pathologically this was a case reported personally to Faust by Carrera in Porto Rico].

The fact that such recorded schistosome infections of the brain other than those by *S. japonicum* appear to be lacking in Africa is attributed by the present author to the possibility that sufficient search has not been made for them and he suggests that a large scale investigation in an endemic area would almost certainly be rewarded.

He then records a case of an African soldier who was brought in dead to hospital in 1942. There were many flukes in the liver and petechiae on the pericardium and peritoneum. The brain and meninges were congested, but there was no evidence of meningitis or malaria. There was what appeared to be a diffuse capillary haemorrhage in the pons, but histologically no extravasation of blood was seen, the capillaries and venules were blocked by thrombus and digestion of the brain-tissue showed *S. mansoni* eggs. A digest of the liver showed *mansoni* and *haematobium* eggs. While the characteristic granuloma surrounding ova in the brain was not present, it is likely that the man died from vascular blockage by an adult fluke or by ova. This is claimed as the first recorded case in which *S. mansoni* ova were found in the brain. The author adds that in seven other attempts to find ova by digestion in different brains the results were negative.

He also quotes a case of another African soldier, with a diagnosis of extra-medullary tumour. No ova were found in the excreta and there was no

according to reports, and a sanitary inspector of the area drew attention to it in 1942, and about the same time the cotton companies of the area noted a heavy mortality due to the condition known locally as *ditola* thought to be schistosomiasis.

Snails of various genera were found in the numerous streams of the country the most common were of the genera *Planorbis*, *L. macra*, *Lamides*, *Physa* and *Physa*. The species of *Planorbis* were *P. (Biomphalaria) edwardsi* or *P. (Afroplanorbis) salinarum*, and in one place the large *P. (Afroplanorbis) tanganykanus* was taken [see also this Bulletin 1947 v 44 825].

The author digresses from his main theme to discuss *ditola*, which is probably the same as the *ditola* or *madidi* described by PIERAULTS [see this Bulletin 1942, v 39 99 1947 v 44 225], and is characterized by depigmentation of skin and hair, anemia and oedema. It is a disease of the very poor and is probably associated with severe malnutrition and hookworm infestation, but the name may be applied by the Africans to a variety of severe chronic illnesses and schistosomiasis is probably a factor in some cases.

In a table the author summarizes the findings of the three medical auxiliaries during the years 1943-45 when some 172,000 persons were examined. In 1943 the rate was 29.8 per cent. and in the two succeeding years 15.7 and 15.8 per cent. respectively.

He remarks that the true incidence must be higher probably much higher than this because as a rule only one specimen was taken from each person, and concentration methods were not used. In one area the reported figure was 69 per cent., and there were considerable differences between the rates in different places. As a rule the rates in adults were considerably higher than in children. Hookworm infestation was present in 26.6 per cent. of those examined in one large area. In certain places on the edges of the Lubilash area the incidence of schistosomiasis was much lower below 2 per cent.

The author's team which included Dr MURRAY, a medical auxiliary and 5 microscopists, made a survey of 1,829 people in 9 places, examining one specimen from each person: the incidence of intestinal schistosomiasis ranged from 1.4 to 14.9 per cent. (except in one district of 50 per cent.) and of hookworm from 36 to 66 per cent. In general the infections were fairly light.

Of other diseases pulmonary tuberculosis is the most serious: it is not perhaps very common, but persons with positive sputum are reported regularly by medical men in the neighbourhood. Trypanosomiasis was found in 0.4 per cent. of 6 or 100,000 examined during 1948 (not by the author) but in one village 15 per cent. of the inhabitants were new cases. Leprosy and syphilis occur and also onchocerciasis with blindness.

There are 10 dispensaries, some built by the cotton companies, some by the government and one by a mission.

In a final note the author makes the point that schistosomiasis is a disease of adults: that up to 50 per cent. of the people are infected in some places but that the infection is usually light. His remark that in studying the Africans it is necessary to go to their own village since if the people are required to travel far to an examination centre the very sick cannot do so and some others will not. He suggests that an autonomous medical mission could be formed to study and deal with these remote people and to examine them all in their own place and that it should consist of 4 medical men and 6 auxiliaries (the precise status of whom is not given) they report daily for pay. For the hospital and laboratory needed for such a mission an initial sum of 3,000,000 francs and the annual sum of the same amount would be necessary. In a postscript he states that the government agrees with his suggestion but that the government organizations will probably carry out the work.

Charles H. Woods

FERRO-LUZZI, G. Studio sulla bilarziosi intestinale da *Schistosoma mansoni* in Eritrea [*Schistosoma mansoni* Infection in Eritrea] *Boll Soc Ital di Med e Igiene Trop* (Sez Eritrea) 1948, v 8, Nos 1/2, 5-18, 2 figs [12 refs] English summary

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H Harold Scott

RAPER, A. B. Cerebral Schistosomiasis [Correspondence] *East African Med J* 1948, June, v 25, No 6, 262-3

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He then records a case of an African soldier who was brought in dead to hospital in 1942. There were many flukes in the liver and petechiae on the pericardium and peritoneum. The brain and meninges were congested, but there was no evidence of meningitis or malaria. There was what appeared to be a diffuse capillary haemorrhage in the pons, but histologically no extravasation of blood was seen, the capillaries and venules were blocked by thrombus and digestion of the brain-tissue showed *S. mansoni* eggs. A digest of the liver showed *mansoni* and *haematobium* eggs. While the characteristic granuloma surrounding ova in the brain was not present, it is likely that the man died from vascular blockage by an adult fluke or by ova. This is claimed as the first recorded case in which *S. mansoni* ova were found in the brain. The author adds that in seven other attempts to find ova by digestion in different brains the results were negative.

He also quotes a case of another African soldier, with a diagnosis of extra-medullary tumour. No ova were found in the excreta and there was no

cosinophilia. Laminectomy revealed the presence of a dense plaque of fibrous tissue compressing the cord—removal resulted in complete recovery. Section showed that the fibrous tissue had been laid down around an adult *E. coli* calcification was considerable so that the species could not be identified. Ten years previously the patient had first experienced pain in the legs and difficulty in walking—later a spastic paralysis had developed. It is suggested that the initial acute lesion had corresponded with the arrival of the adult worm in the spinal canal.

H. J. O. D. Burke-Gifford

WATSON, J. M., ABDEL AZIM, M. & HALAWA, A. Investigations on the Antibilharzial Action of Miracid D (Miledin). *Trans. Roy. Soc. Trop. Med. & Hyg.* 1948, July v 42, No. 1 32-34 1 pt. [29 refs.]

Miracid D is a new drug for the treatment of schistosomiasis. It is 1-methyl-4-diethylaminoethylaminothioxanthone hydrochloride [see this *Bulletin*, 1948, v 43 326].

In patients treated in Egypt toxic effects (if present) were slight and transient. The commonest were anorexia, nausea and vomiting. In a few cases vertigo, tremors, and tinnitus occurred. Heart, liver and kidney functions, and blood pressure were normal. There were no significant changes in the blood apart from some increase of eosinophilia. A few patients showed idiosyncrasy marked by lassitude, restlessness, insomnia, nausea, metallic taste, tingling of the skin, headache and lumbar pain.

Experiments were first carried out on mice, and gerbils infected with *S. mansoni*. The results obtained (for which the original paper should be consulted) confirmed Hiketh's reports. To kill all the worms it was necessary to give six daily doses of 40 mgm. per kgm.

The first group of 20 patients contained 14 *S. haematobium* infections, 2 *S. mansoni* infections and 4 double ones. They were given 2 doses of 0.4 gm. (7.10 mgm. per kgm.) with an interval of 3 days, and they were observed for 4-67 days. Four of the 6 *S. mansoni* infections and three of the 18 *S. haematobium* ones seemed to have been cured.

The second group contained 13 patients infected with *S. haematobium* who were given 3 doses of 0.4 gm. (stated per kgm. but presumably per person) at intervals of 3 days. They were observed for 5 to 70 days, during which period 2 ceased to pass viable ova, i.e. they may have been cured.

The third group consisted of 4 patients infected with *S. mansoni*. They were given 0.4 gm. per patient on 4 alternate days and were observed for 50 days after which time only 1 patient was still passing viable ova. They were then given a second course consisting of 0.4 gm. on 5 successive days, after which the excretion of viable ova ceased.

The fourth group consisted of 6 children infected with *S. haematobium*. They were given 0.1-0.3 gm. every twelve hours for 3-6 days. In 1 week later the urines still contained living eggs and a second course with doses of 0.1-0.3 gm. was given. In 2 months continued to be passed although the proportion of degenerate ones increased.

A fifth group of 6 cases was treated with miscellaneous drugs and in most of them a temporary cessation of the secretion of eggs occurred.

A sixth group consisted of 14 patients who received 1.5 mgm. per kgm. every 12 hours if the urinal clearance was above 50 and 3 mgm. per kgm. if it was below. Treatment was continued for 3-7 days. A fortnight later all were still passing eggs.

It is concluded that Miracid D is effective against both *S. haematobium* and *S. mansoni*. It is suggested that different total doses, administered at different

sufficiently short period, but although marked improvement is apparent, complete cure is not usually attained [by the dose schedules described in the present paper]

[The patients described in this paper seem to form an earlier series than those reported by HALAWANI, *et al*, this *Bulletin*, 1948, v 45, 797) in which doses up to 7.5 gm during 8 days were employed, these doses cured 2 out of 3 patients BLAIR, HAWKING, MEESER and ROSS (in press) have found in Southern Rhodesia that when children infected with *S. haematobium* were given 10 mgm per kgm daily for 10 days, 12 out of 18 were cured (15 weeks observation), some adults tolerated doses up to 1.6 gm per person daily] F Hawking

ATKINS, W R G A Suggested Repellent for Schistosome Cercariae *J Hygiene* 1947, Dec, v 45, No 4, 468

In this brief note the author suggests that copper soaps—particularly the greasy copper oleate alone or mixed with the firmer copper stearate or palmitate—may be effective repellents for schistosome cercariae. He has not tried them but suggests that experiments could be made at those bathing beaches in America where schistosome dermatitis is common. Copper is apparently more poisonous than mercury to certain worms (not pathogenic for man). If the soaps prove to be effective, they could be used by engineers, fishermen, and others working in water. Unguentum cupri oleatis B P C is 12½ per cent copper oleate in soft paraffin, it is unlikely either to irritate the skin or to be absorbed through the skin in toxic quantity Charles Wilcocks

FIRLOTTE, W R A Survey of the Parasites of the Brown Norway Rat *Canadian J Comp Med* 1948, July, v 12, No 7, 187-91 [22 refs]

The author, in the Institute of Parasitology, McGill University, Macdonald College, Quebec, examined 150 specimens of *Rattus norvegicus* for parasites. The results are given in detail, and show that many species of parasites were found—the only ones of interest in human medicine, however, were *Hymenolepis diminuta*, *Capillaria hepatica* and, possibly, *Hymenolepis murina*, which were found respectively in 4, 6, and 16.5 per cent. *Capillaria hepatica* was diagnosed entirely by the finding of the characteristic eggs in the contents of the large intestine H J O'D Burke-Gaffney

COITO, A de M Contribuição para o estudo da epidemiologia do quisto hidático humano em Portugal Sobre o grau de infestação dos cães errantes de Lisboa pela *Echinococcus granulosus* [The Epidemiology of Hydatid Cysts in Man in Portugal Infection Rate of Stray Dogs in Lisbon with *Echinococcus granulosus*] *An Inst Med Trop* Lisbon 1947, Dec, v 4, 285-95 [19 refs]

The English summary appended to the paper is as follows—  
“Studying the epidemiology of the human Hydatid Cyst in Portugal the author determined the rate of infestation by *Echinococcus granulosus* of the street dogs at Lisbon.  
At first he refers to the number of hydatid cyst cases registered in the two largest hospitals of Lisbon, during the period 1934-1943, the mean number of cases being 35.5 (0.11 per cent of the patients) for the Civil Hospitals and 5.2 (0.16 per cent of the patients) for the Hospital of the Medical School.  
In addition the author points out that in the 150 dogs observed he found infested by *Echinococcus granulosus* (3.3 per cent) and only 12 of those animals were not infected by helminths.”

eosinophilia. Laminectomy revealed the presence of a dense plaque of fibrous tissue compressing the cord. Removal resulted in complete recovery. Section showed that the fibrous tissue had been laid down around an adult male calcification was considerable so that the species could not be identified. Two years previously the patient had first experienced pain in the legs and difficulty in walking. Later a spastic paralysis had developed. It is suggested that the initial acute lesion had corresponded with the arrival of the adult worm in the spinal canal.

H. J. O'D. Burke-Gaffney

WATSON, J. M., ABDEL AZIM, M. & HALAWANI, A. Investigations on the Antihelminthic Action of Miroal D (Mirodin). *Trans. Roy. Soc. Trop. Med. & Hyg.* 1948, July v. 42, No. 1, 37-54, 1 pl. (29 refs.)

Miroal D is a new drug for the treatment of schistosomiasis. It is 1-methyl-4-diethylaminoethyl-laminothiazanthione hydrochloride (see this *Bulletin* 1948, v. 45, 526).

In patients treated in Egypt toxic effects (if present) were slight and transient. The commonest were anorexia, nausea and vomiting. In a few cases vertigo, tremors, and tinnitus occurred. Heart, liver and kidney functions and blood pressure were normal. There were no significant changes in the blood apart from some increase of eosinophilia. A few patients showed idiosyncrasy marked by lassitude, restlessness, insomnia, nausea, metallic taste, tingling of the skin, headache and lumbar pain.

Experiments were first carried out on mice, and gerbils infected with *S. mansoni*. The results obtained (for which the original paper should be consulted) confirmed Hiketh's reports. To kill all the worms it was necessary to give six daily doses of 40 mgm. per kgm.

The first group of 20 patients contained 14 *S. haematolum* infections, 2 *S. mansoni* infections and 4 double ones. They were given 2 doses of 0.4 gm. (7-10 mgm. per kgm.) with an interval of 3 days, and they were observed for 4-67 days. Four of the 6 *S. mansoni* infections and three of the 18 *S. haematolum* ones seemed to have been cured.

The second group contained 12 patients infected with *S. haematolum*, who were given 2 doses of 0.4 gm. (stated per kgm. but presumably per person) at intervals of 3 days. They were observed for 5 to 10 days, during which period 2 ceased to pass viable ova, i.e. they may have been cured.

The third group consisted of 4 patients infected with *S. mansoni*. They were given 0.4 gm. per patient on 4 alternate days and were observed for 50 days after which time only 1 patient was still passing viable ova. They were then given a second course consisting of 0.4 gm. on 5 alternate days, after which the excretion of viable ova ceased.

The fourth group consisted of 6 children infected with *S. haematolum*. They were given 0.1-0.3 gm. every two hours for 5-6 days. Ten weeks later the worms still contained in the eggs and a second course of 0.2-0.3 gm. was given. Living ova continued to be passed although the proportion of degenerate ones increased.

A fifth group of 6 cases was treated with nine flaccid doses and in most of them a temporary cessation of the excretion of ova occurred.

A sixth group consisted of 14 patients who received 3 mgm. per kgm. every 1 hour if the ova clearance was above 50 and 3 mgm. per kgm. if it was below. Treatment was continued for 5-7 days. A fortnight later all were still passing living ova.

It is concluded that miroal D is effective against both *S. haematolum* and *S. mansoni* provided that sufficient total dosage is administered during



## Helminthiasis

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Other physical signs included transient swelling and localized lymphoedema, urticaria, conjunctivitis, and mental manifestations, mainly anxiety states. "Filarial fever" was not reported in early cases. In a few instances abscesses were reported, these were presumed to be filarial in origin. There was no evidence of sexual dysfunction.

"Attacks" were nearly always short, 3 to 5 days in duration, in many instances the signs and symptoms had disappeared in a matter of hours, and very rarely they lasted for longer than 2 weeks [except presumably the mental symptoms]. Relapses were relatively common, they were precipitated by hard exercises, fatigue, and hot climate, they occurred up to two years after infection. Lymphatic lesions in the experience of most writers persisted for some time after the return of the men to the United States, but having eventually subsided were seldom found after 20 months to 3 years, according to different observers, from the time the subject left the endemic area.

There are reports of the finding of microfilariae in the blood in 20 cases only; this includes one instance in which positive findings in 8 cases were reported, whereas 13 authors report no positive findings. In a total of 364 biopsies, adult worms or microfilariae were found in 78 (22 per cent). The adults were all identified as *W. bancrofti*. Bacterial cultures of biopsies were almost without exception negative.

The white cell count averaged 9,000 per cmm and eosinophilia occurred in one-half to two-thirds of the cases, averaging 850 per cmm. The blood sedimentation rate was usually unchanged.

Positive intradermal tests varied from 35 per cent to 91 per cent but most writers reported percentages above 80. *Dirofilaria immitis* was used for preparing the antigen in most instances. False positives were uncommon, usually of the order of 5 per cent, the test was only considered positive if both immediate and delayed reactions were noted. The reaction appeared early, usually prior to the first symptoms. Antigens made from other filarial worms, e.g., *Setaria equina*, *Litomosoides carini*, and the microfilaria of *W. bancrofti*, were also used with very similar results. Tests with antigens prepared from other nematodes, e.g., *Ascaris*, gave less satisfactory results.

There is a detailed description of the pathological findings in biopsies from various sites including the epididymis, spermatic cord, testis, lymph nodes from various places, with and without worms, and lymph vessels. These are also presented in tabular form and are illustrated by beautiful photomicrographs. In ten lymph nodes adult worms were found, in 23 characteristic histological changes were found in the absence of worms, and in 24 others neither worms nor characteristic lesions were found. The following summary of the histological findings is quoted —

"It is interesting to make a comparison of the tissue reactions associated with adult worms, and with microfilariae. In the former there is precipitation of strongly acidophilic material about the worms with necrosis of tissues, exudation of eosinophils, plasma cells and lymphocytes, and proliferation of macrophages and reticular fibers. In the latter there is no necrosis and the precipitate around the microfilariae, when it occurs, is amphoteric. Edema is conspicuous and the exudate is comprised chiefly of eosinophils. Macrophages and giant cells, although present, are not numerous and there is only slight reticular hyperplasia."

With reference to pathogenesis, two relevant quotations from the "Discussion" are given below —

"As a result of the war experience clear evidence has accumulated that early filariasis is due solely to *W. bancrofti* and is not caused by bacteria or conditioned by their presence. Even after many months bacteria have not entered into the picture. Much other evidence indicates that *W. bancrofti* is

OKY OKY BIK. Een geval van Ileus door Ascariëden veroorzaakt. [A Case of Intestinal Obstruction caused by *ascaris*.] *Med Maandblad Batavia*, 1948 July 1 No. 74 488-9.

The English summary appended to the paper is as follows:—

"Description of a case of intestinal obstruction due to *Ascaris lumbricoides* in a 3 years old Indonesian girl.

"The mass of worms which was located in the last 30 cm. of the ileum, near the ileo-caecal valvula, consisted of 68 *Ascaris lumbricoides* (27 male 39 female) and was removed by operation. Diagnosis as to the cause of obstruction could not be made before operation.

ERNHARDT A. Ueberblick ueber die medikamentöse Therapie der Ascaridose. [A Review of the Therapeutics of *ascaris* Infections.] *Med Abn.* 1948, F b v 43 No 4 114-17 [34 refs.]

WARTMAN W. B. Filariasis in American Armed Forces in World War II. *Medicine* 1947 Dec. v 26, No. 4 333-84 33 figs. [55 refs.]

Pathological material, all from biopsies, was collected from every available source for the U.S. Army Institute of Pathology—this forms the basis of the report. The clinical picture is drawn from numerous published reports and refers only to soldiers, sailors and marines in the U.S. services.

The patients were nearly all young men between the ages of 18 and 24. Most were infected in the Samoan Islands the number from Walis Island being unusually high. A few were infected elsewhere (e.g. in the Solomon Islands). The average time spent in an endemic area was 11 months and the shortest time was one month. The usual incubation period was from 5 to 18 months but adult worms were recovered in biopsy material within 3 months of the first exposure.

The onset was usually manifested by painful swelling of the scrotal contents, arms and legs, either singly or in combination. Frequently the affected parts were swollen red and itched, and at times wheals were noticed. Although headache, backache, fatigue and nausea were common, other constitutional symptoms such as fever, chills and malaise were unusual. Subjective symptoms were prone to develop suddenly, were mild to moderate in severity, often fleeting, and were characterized by remission and exacerbation. Often patient had no symptoms at all and the disease was accidentally discovered during the course of a routine physical examination. In evaluating these symptoms it should be remembered that they were tabulated from statements made by the patients themselves, many of whom were suffering from built fatigue or had considerable anxiety or even fear about the outcome of their disease—the statements were no doubt influenced by these factors.

The most frequently encountered physical signs were lesions of the genitalia. Of these the commonest were funiculitis, epididymitis, orchitis and scrotal oedema and inflammation. Itching and varicose were also fairly common, but chloasma hydrocele and elephantiasis were rare.

Lymphadenitis was the next most constant sign—the commonest groups were the inguinal, femoral, axillary and palmar. In few instances the cervical glands were involved and rarely the subclavicular, popliteal and pectoral. Few other reports of generalized lymphadenitis.

Retrograde lymphangitis was common but far less common than lymphadenitis, in which it was usually associated. Occasionally it was not associated with adenitis. The same as it was mainly in the distal. There was erythema, induration and the associated pain was minimal.

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## Deficiency Diseases

This observation confirms previous experiments and indicates that *Culex pipiens* var *pallens* is a poor intermediate host of *W. malayi* L E Napier

TOWNE C E Surgery of Elephantiasis of the Scrotum of Filariar Origin New England J of Med 1948, Aug 5, v 239 No 6, 223-6, 1 fig

BROSIOUS, O T, THOMAS, Esther E & BROSIOUS, Barbara Capillaria hepatica A Case Report Trans Roy Soc Trop Med & Hyg 1948, July, v 42, No 1, 95-7

Record of the case of a woman in Panama, 28 years of age, suffering for 4 days from very acute epigastric pain at short intervals accompanied by nausea and once by vomiting. In the stool were ankylostome and *Capillaria hepatica* ova. The family lived largely on "wild meat", including conejo pintada, a small amphibian rodent, and venison and birds, she was very partial to liver of the former. She denied eating peccary (an animal infested in nature by *Capillaria hepatica*) or monkey (the red spider monkey, *Ateles geoffroyi*, and the white-faced monkey, *Cebus capucinus imitator*, are both hosts of the *Capillaria*). The pain was relieved by morphine, oil of chenopodium was given for the hookworm, subsequent stool examinations failed to reveal any ova of *Capillaria hepatica* H Harold Scott

ERHARDT, A E Kritischer Beitrag zur Behandlung der Oxyuriasis [Critical Review of the Treatment of Enterobiasis] Med Klin 1947, Dec, v 42, Nos 23/24, 859-61 [23 refs]

The author refers in this brief article to more than a score of vaunted remedies for *Enterobius* infestation. In assessing their value, one must be careful to distinguish relapse which may occur up to 8 weeks after the remedy is used (and implies failure to eradicate) and reinfection, indicated by appearance of ova in the stools later than this. He speaks most highly of Lubisan, resorcin-mono-butyl-ether-diethyl carbamate, which, according to report, succeeds in about 75 per cent of cases. For many drugs of repute—helminal, butolan, santonin, ascaridol, gentian violet, among others—he has not a good word to say. He concludes that up to the present there is no absolutely reliable remedy, that all we can do is to treat symptoms, apply measures to prevent infestation or re-infestation, and that in time the infestation will clear up of itself [Not very helpful, but probably quite true. A useful survey] H Harold Scott

PIAGGIO BLANCO R A, FERNÁNDEZ CHAPELA, A. & PASEYRO, P Triquinosis [Trichinosis] An Facul de Med Montevideo 1948, v 33, Nos 1/2, 135-60 [67 refs]

A general review and account of a case

## DEFICIENCY DISEASES

DRILL, V A & LOOMIS, T A Production of Functional and Fatty Changes in the Liver by a Chronic Vitamin B Complex Deficiency and Interrelationships with Protein Intake J Nutrition 1948, Mar 10, v 35, No 3, 333-48, 6 text figs & 8 figs on 1 pl [21 refs]

Liver damage has been produced in animals both by diets deficient in protein and by diets deficient in vitamins of the B complex. Often, however, the experimental conditions have not made it possible to distinguish between the effects

the etiologic agent such as the demonstration of adult and larval parasites accompanied by significant lesions in involved tissues the results of intradermal testing and the clinical manifestations of the disease."

"Many clinical manifestations of early filariasis such as blotchy redness of the skin absence of severe constitutional symptoms blood eosinophilia, and rapid appearance and disappearance of symptoms, are suggestive of hypersensitivity. During attacks of acute lymphangitis in one extremity there is not infrequently enlargement of lymph nodes in distant parts of the body such as the neck, groin or opposite extremity. The high incidence of positive skin tests desensitization, passive transfer experiments and reproduction of some of the characteristic signs and symptoms by intradermal injection of a suitable antigen can all be explained on this basis.

[The paper as a whole constitutes a most important document on the early manifestation of filariasis and should be studied in the original.]

L. E. Naper

CHEN H. C. A Note on the Filaria Survey in Fukien Province. *Lingnan Sci J* 1943, v 22, Nos. 1/4 85-92, 1 map. [12 refs.]

A questionnaire on the incidence of elephantiasis in Fukien province was sent out. The disease was reported in 38 *hsien*s in 14 of which it was especially prevalent. From 25 *hsien*s it was reported as absent.

Microfilarial surveys were carried out on a number of places in the province blood specimens were taken between 9 p.m. and 11 p.m. The findings in the different locations are discussed in detail. In Foochow hospital patients in whom the infection was suspected were examined and 40.1 per cent of 207 patients were found infected. Many of these came from outside Foochow (in about one-third of the cases) *W. wuxi* was found. In other places unselected prisoners, students or members of volunteer corps were examined. The microfilarial incidence varied from 30.0 per cent (Changpu) to nil (Yungau and Shashien). Incidences above 10 per cent were found in Futun (25.1 and 19.4 per cent) Putien (14.5 per cent) and Haileng (1 per cent).

The correlation between microfilaraemia and elephantiasis is not discussed, but the two *hsien*s showing no microfilaria do not appear in the list of those reporting elephantiasis and of the three *hsien*s showing the highest microfilarial incidence two appear in the list of those with especially prevalent elephantiasis.

*W. wuxi* was diagnosed in about one-fifth of the positive cases in the non-hospital groups this infection is apparently widespread in the province.

A map shows the distribution of filarial infection as occurring along the coast-line and in the riverine areas.

L. E. Naper

HU S. M. H. Notes on the Experimental Infection of *Culex pipiens* var *pallens* Coq. with *Microfilaria malaysi* Brug. *Lingnan Sci J* 1943, v 22, Nos. 1/4 79-83.

In Shanghai between September 13th and 24th 1940 *Culex pipiens* var *pallens* were fed in three batches on a patient heavily infected with *M. malaysi*. The average blood microfilaria counts during the times of feeding varied between 323 and 5.1 microfilariae per mm. of blood.

In a total of 247 mosquitoes dissected between the 8th and 30th days after the infective feed, filarial larvae developed to the infective stage in only 5 (2.03 per cent) and in each case there were only very few larvae. In 20 other mosquitoes immature larvae were found all of these except one were dead or completely encapsulated, and the remaining one had reached the second stage.

This observation confirms previous experiments and indicates that *Culex pipiens* var *pallens* is a poor intermediate host of *W. malayi* L E Napier

TOWNE, C E **Surgery of Elephantiasis of the Scrotum of Filarial Origin** New England J of Med 1948, Aug 5 v 239, No 6, 223-6, 1 fig

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A general review and account of a case

## DEFICIENCY DISEASES

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Liver damage has been produced in animals both by diets deficient in protein and by diets deficient in vitamins of the B complex. Often, however, the experimental conditions have not made it possible to distinguish between the effects

of these two deficiencies. One reason for this is that the appetite is often impaired, and with reduced food consumption there is inadequate intake of all nutrients. The experiments reported here were designed to overcome these difficulties. A chronic deficiency of the whole vitamin B complex was produced in dogs; the food intake was measured, and a control group was pair fed, but given an adequate vitamin supplement. In this way the effect of inanition *per se* could be determined. To test the possibility of an interaction between protein and B vitamins in their effects upon the liver the experiments were carried out at two levels of protein intake—normal (20 per cent. casein) and high (41 per cent. casein). Liver function was studied by serial measurements of bromsulphthalein retention and of serum phosphatase. These tests were chosen because they are in common clinical use. A single biopsy of the liver was made in each animal after about 30 weeks.

On the high protein diet the vitamin-deficient animals had reduced appetite and lost weight. No histological or functional changes were found in the liver. In one dog there was proliferation of the capsular epithelium and crescent formation in the renal glomeruli. On the 20 per cent. casein diet vitamin deficiency produced an increase in bromsulphthalein retention and serum phosphatase concentration. Biopsies of the liver taken at the 33rd week showed a moderate degree of fatty infiltration.

[The photomicrographs of these biopsies show a striking resemblance to that published by SERRELL in his description of the "yellow liver" of anabellous in the dog (SERRELL, 1933 *Nat Inst Health Bull.* No. 16, p. 23).]

After the biopsies the dogs were given an adequate vitamin supplement but kept on a restricted food intake. When they were killed 10 weeks later the livers were normal. In the inanition controls there were neither functional nor histological changes in the liver.

[These experiments have an obvious bearing on problems of human disease that have been discussed in recent numbers of this *Bulletin*. But it must always be remembered that, in the field of nutrition the results obtained on one animal cannot be applied without reserve to another. It would be dangerous to conclude that in man avitaminosis can cause liver damage in the presence of a normal supply of protein. The authors do not imply this, but the discussion they give of their results is confusing.]

Although in the dog both protein- and vitamin-deficiency may cause liver damage the former seems to be the more powerful factor. In dogs given a very low protein diet with adequate vitamin liver damage was much more severe and rapid in onset than that described above. (L. & FREEMAN 1947 *J. Physiol.* 1948, 145, 646-53.) J. C. HAZEL

FERRO-LIZZI G. Studio sui fenomeni di malnutrizione in Eritrea. Nota IIIa. Ricerche sperimentali su diete a base di dura (*Andropogon sorghum*) di taff (*Eragrostis abyssinica*) e di orzo. Nutrition Studies in Eritrea. III. Experimental Research with *Inde pagon* *ochum* *Egypti* & *orzo* and Barley. *Bull Soc Ital di Med Igiena Trop* (New Eritrea) 1948, 8, Nos 1-2, 54-61.

The numbers of animals subjected to experiment—about 1 of 20-300 gm. weight—were few from which to draw and deduct any. Five (1 male 4 females) were fed on taff (inde p. *ochum*) only, nine (5 males 4 females) on dura (*Eragrostis abyssinica*) only, and 4 males on barley only. 19 animals altogether. 10 lived for 1 month, nine for 9 months, one for 6 months and two for 3 months only, one escaped after 6 months. Eleven were killed in the course of the investigations & died of disease. All shown *deh.* of *malnut.* and interference with fertility.

The author came to the conclusion that the effects were not the result of avitaminosis but of protein deficiency, especially amino-acids, in other words, the proteins in these pulses are of "poor biological value", and unable to maintain a satisfactory nitrogen balance. Control animals receiving fresh vegetables in addition showed no signs of malnutrition.

H Harold Scott

ALTMANN, A. The Syndrome of Malignant Malnutrition (Kwashiorkor Infantile Pellagra) Its Conception as a Protein Deficiency and Its Treatment with Skimmed Lactic Acid Milk. *Clin Proc Cape Town* 1948, Jan, v 7, No 1, 32-53 [84 refs]

Thirty cases are described of kwashiorkor in Bantu babies and children varying in age from three months to six years. They presented the characteristic clinical picture—loss of weight, dermatosis, lesions of mucocutaneous junctions, depigmentation of the hair, oedema, hypoproteinaemia, and normocytic anaemia of moderate severity. Although all cases had the typical rash, the author believes that this and other signs of vitamin deficiency are not essential features of the disease, they are not always present, and bear no relation to the severity of the individual case. He contends that the main cause of the syndrome, which is in no way peculiar to the Bantu, is lack of protein and lack of calories, and that it closely resembles the condition known to paediatricians in Germany as *mehlnährschaden*, or "flour-feeding injury".

In kwashiorkor, as in *mehlnährschaden*, there is a history of feeding on a mainly carbohydrate diet. In both there is oedema and fatty liver. The classical descriptions of *mehlnährschaden* mention muscular rigidity, which is not uncommon feature of kwashiorkor. In some cases there is a reddish-brown pigmentation of the skin, which may be analogous to the kwashiorkor dermatosis. If kwashiorkor, like *mehlnährschaden*, is a result of protein deficiency, it should be cured by a high protein diet. Dr Altmann points out that "when using a therapeutic formula in nutritional disorders of babies, it is not only important to choose the correct formula, but also to apply it correctly". The food he suggests is lactic acid skimmed milk. This was given in small quantities at first, increasing daily until 30-35 oz were taken in 24 hours. On this treatment it was found that the frankly oedematous patients did well, there were 22 cases of this type, and all recovered. The prognosis was much worse in those who were dehydrated or atrophic [the terms seem to be used synonymously]. Of 8 such cases, 5 died. No details of post-mortem findings are given.

The paper ends with a long and fully documented discussion, devoted mainly to oedema, the significance of fatty liver, and the results of treatment. Oedema is not an essential part of the syndrome, since the most serious cases are those in which it is absent or minimal. Nor is fatty liver pathognomonic of kwashiorkor since it is found in infants dying of many other conditions. Even when fatty infiltration is present, there is no evidence that it causes serious functional impairment or that death occurs from liver failure.

[Recent work on kwashiorkor is in agreement with Dr Altmann's main conclusions—that the condition is a result of protein deficiency, that the signs of avitaminosis are inessential complications, and that there is a good response to treatment with milk alone.] The comparison with *mehlnährschaden* has been made by others, but not so fully. It is of value, because it lifts kwashiorkor out of the realm of purely tropical diseases, and brings it into relation with the existing body of knowledge about the nutritional disorders of infants in temperate countries. This knowledge is far from complete, and will in turn be amplified by the work on kwashiorkor. If this position is accepted, it is only

logical to apply to kwashiorkor the classical principles of feeding evolved by paediatricians for the treatment of infantile malnutrition. Dr Altmann is the first to do this explicitly.

Some of his conclusions on other points are, perhaps, open to criticism. He distinguishes between oedematous and dehydrated cases—reference to his tables shows that in all the dehydrated cases oedema was said to be present, comparable in severity and extent to that found in the waterlogged patients. There was also an equal reduction in the serum proteins—in 4 out of 6 dehydrated cases the total protein was less than 4.0 gm. per cent. It therefore seems reasonable to look upon this dehydration not as a difference in kind, but as a complication, which, as in other diseases of infancy is of grave omen.

The contention that liver function is not affected by the presence of fat cannot be accepted without reserve. Experimentally functional impairment has been found in rats (Macleod *et al.* *Brit. J. Exper. Path.* 1937 v 18, 345) and in dogs (above) with fatty livers. It has also been reported in human infants since Dr Altmann's paper was published (Waterlow *this Bulletin* 1948 v 43 774). There are several observations in the literature of sudden death in coma in kwashiorkor which are suggestive of death from liver failure (see Huguenz *ibid* 1948 v 43 768).

J. C. Waterlow

ALTMAN R. J. & STOLLERMAN G. H. The Course of Beriberi Heart Disease in American Prisoners-of War in Japan. *Ann. Intern. Med.* 1948, May v 28, No. 5, 949-8, 3 figs. (28 refs.)

FLACHS A. Nicotinamidetreated pellagrous diarrhoea ("pellagra sine pellagra"). [Nicotinamide Treatment of Pellagrous Diarrhoea, "Pellagra sine Pellagra."] *Nordisk Med* 1948, Aug. 15 v 39 No. 33, 1507-9 (23 refs.)

The English summary appended to the paper is as follows:—

"22 cases of diarrhoea observed in the medical department of the Old People's Home at Copenhagen were treated with nicotinamide. All the cases had been treated previously with the ordinary obisipants without effect. None of the patients except 2 had had cutaneous pellagrous manifestations. In 17 cases the nicotinamide therapy proved successful. In one of the cases that did not respond to the specific therapy autopsy revealed a cancer of the colon. A dose of 15-30 mg. nicotinamide per day was given and effects could be observed after 1-3 days. A case of anabolic leucosis is described in which treatment with lactoflavin led to an outbreak of pellagrous diarrhoea and the author points out the antagonistic action of the vitamins of the B group."

## SPRUE

INNES Elizabeth M. The Blood and Bone Marrow in the Sprue Syndrome. A Study of 63 Cases. *Edinburgh Med. J.* 1948, May v 53 No. 3 202-12 (19 refs.)

From a review of the literature it is evident that the frequent occurrence of megaloblastic anaemia among cases of tropical sprue has been established. On the other hand, the blood picture in the sprue syndrome as met with in Britain is much less well-defined.

Sixty-three cases of the sprue syndrome have been studied. Seventeen could be classified as tropical sprue 27 as non-tropical sprue and 19 as coeliac disease. It appears clear that the adult sprue syndrome is typically associated with



macrocytosis of the erythrocytes which may be accompanied by anaemia, but sometimes not. This statement applies equally to tropical as well as non-tropical sprue. The difference between them is one of degree, as the tendency to anaemia and macrocytosis is greater in the non-tropical group, but the bone marrow picture is characteristically megaloblastic when there is a marked degree of macrocytic anaemia. Occasionally this megaloblastic reaction may prove completely refractory to parenteral liver therapy, though usually this will improve the blood level and change the marrow picture either to the normoblastic or intermediate state. It would appear that the administration of liver results in a partial maturation of the megaloblasts. The process is, however, not complete and stops short of a complete transformation to the normoblastic state. The erythrocytes which result are reduced in numbers and are larger than normal, a fact which explains the persistent macrocytosis so characteristic of this condition. It is therefore suggested that some other factor is necessary for the complete restoration of normal erythropoiesis, the nature and identity of this factor is unknown. In some cases, the factor might be folic acid, but in others the macrocytic anaemia persists despite its prolonged administration.

Macrocytic megaloblastic anaemias are extremely uncommon in childhood, so that it is not surprising to find among children with coeliac disease that the anaemia is characteristically of the hypochromic microcytic variety. In this case the marrow is normoblastic and appears capable of producing adequate numbers of erythrocytes, the defect being in their haemoglobinization, but the cases failed to respond to the therapeutic administration of iron—a phenomenon which could be explained either by failure of absorption of iron from the bowel or by failure on the part of the marrow to utilize it.

In this series one patient with coeliac disease responded excellently to intravenous injection of "Ferrivenin" (a proprietary preparation of saccharated oxide of iron). Therefore it is suggested that parenteral iron therapy may prove of great value in the cure of the iron-deficient anaemia of coeliac disease which persists despite prolonged oral administration long after the signs and symptoms of the syndrome have disappeared.

The two most urgent problems for solution are (1) the nature of the factor required for complete restoration of normal erythropoiesis in cases of sprue partially refractory to liver extract and folic acid, and (2) the mechanism underlying the failure of hypochromic anaemia of coeliac disease to respond to iron.

P Manson-Bahr

DICK Margaret I B HARRISON Isobel T & FARRER K T H. The Thermal Stability of Folic (Pteroylglutamic) Acid. *Australian J Exper Biol & Med Sci* 1948 May v 26 Pt 3 239-44 4 figs

DICK Margaret I B HARRISON Isobel T & FARRER K T H. The Microbiological Assay of Folic Acid. *Australian J Exper Biol & Med Sci* 1948 May v 26 Pt 3 231-7, 3 figs [17 refs]

## VENOMS AND ANTIVENENES

BOGULT, P. Venins de serpents et antivenenes [Snake Venoms and Antivenenes]. Préface du Professeur Jules BORDET. Collection de l'Institut Pasteur 157 pp., 12 text figs & 4 figs on 2 pls 1948 Paris. Editions Médicales Fluminon [400 fr]

In this interesting memoir the author summarizes the results of researches on snake venom carried out in France and other countries during recent years

After a brief historical account of the effects of snake bite, the venoms of vipers and colubrids are dealt with generally (opisthophis excepted). The mechanisms of biting and the secretion of venom are briefly discussed and there is a very clear account of the present knowledge concerning the chemical structure and enzyme content of venoms and of their action on the enzymes. The action of physical and chemical agents on venoms is also described, and there are chapters on natural and acquired immunity, the treatment of snake bite and the therapeutic uses of venom. There is a short bibliography.

One chapter is of special interest. Therein the author has attempted to classify venoms according to their physiological and pathological properties. After tabulating variants of these properties such as coagulant, anticoagulant, haemolytic, etc. he groups venoms into four categories, namely: (1) Curarising anticoagulants (type *Naja tripudians*) (2) Curarising coagulants (type *Dermaspis tessilis*) (3) Haemorrhagic anticoagulants (type *Buthus nasicus*) (4) Haemorrhagic coagulants (type *Bothrops russellii*). Group 1 contains the venoms of most of the colubrids of Africa and Asia and some of those of Australia. Group 2, the venoms of the Australian colubrids. Group 3, those of the viperines of Africa and America. Group 4 the venom of the viperines of Europe, America, Asia and of the genera *Echis* and *Crotalus* of Africa.

The author points out the close similarity between the toxic actions of venoms and those of certain bacterial toxins with which the venoms appear to form families *naturelle* in spite of their differing chemical and antigenic structures.

The book is extremely well arranged and clearly written and can be thoroughly recommended to all who are interested in snakes and snake venoms.

B. G. Murgath

SARKAR, N. H. Existence of a Cardiotoxic Principle in Cobra Venom. *Ann. Biochem. & Exper. Med.* 1948, Jan. Feb. v. 8, No. 1, 112, 17 figs. [18 refs.]

The author and others had previously observed that isolated frog heart was brought to a stop in systole by perfusion with crude cobra venom, but not by the various products isolated from the venom such as the haemolysin. In the experiments described in this paper the author records the effects of perfusion of crude venom, haemolysin, neurotoxin and choline-esterase upon isolated frog and kitten hearts and the action of crude venom on the circulation of cats (with and without artificial respiration). The author concludes that cobra venom has a definite toxic action on the heart and that neurotoxin, choline-esterase and haemolysin have not. The action of this cardiotoxic factor which the author has labelled cardiotoxin 19 and claims to have isolated in a pure and concentrated form was further examined in isolated frog heart and intact anaesthetized cats. At a concentration equal to half the effective concentration of crude venom the isolated heart was stopped in systole. Intra-pericardial injection of a dose of cardiotoxin (equal to half the effective dose of crude venom) produced gradual fall of blood pressure to zero and loss of respiration. Artificial respiration failed to revive the animal and the heart was eventually stopped in systole.

In a general introduction to his paper the author states that in India 5000 to 100,000 deaths occur every year from snake bite and claims that considerable numbers of deaths occur from the same cause in other countries including Africa and Australia. No author is responsible for the latter statement which is very objectionable and worthy of considerable doubt. It is difficult to accept the author's conclusions on the evidence submitted in the paper. For instance although he states that haemolysin has no effect on the isolated heart he records Table 13

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that a dose of non-crystalline haemolysin in a concentration of 1 in 50 caused a perfused toad's heart to stop in systole, whereas the same dose of crystalline haemolysin had no apparent effect Table VI is headed "Amount of cobra venom required for the cardiac failure as indicated by the fall of B P to zero mm (artificial respiration being used)" In a condition in which shock frequently predominates, measurement of cardiac failure in terms of fall of blood pressure cannot be reasonably accepted However, at high concentrations of crude venom his published charts indicate some action on the heart, and the work should obviously be repeated more carefully in order to ascertain whether this effect is in fact due to a specific cardiotoxic principle ] B G Macgregor

TRETHEWIE, E R & DAY, A J The Influence of Heparin on the Toxicity of Australian Snake Venom *Australian J Exper Biol & Med Sci* 1948, Jan, v 26, Pt 1, 37-43, 2 figs

Other workers have shown that heparin significantly reduces the toxicity of the venoms of the *Echis carinatus* and *Vipera russelli* [this *Bulletin*, 1947, v 44, 846], both of which have coagulant effects The authors report the results of an investigation of the effects of heparin on the thrombotic activity of the venoms of two Australian snakes, *Notechus scutatus* and *Pseudechis porphyriacus* Tiger snake (*Notechus scutatus*) venom was injected subcutaneously into guinea-pigs in about double the LD<sub>50</sub> dose and heparin was injected immediately afterwards and thereafter daily Control series were injected with venom alone Venom of *Pseudechis porphyriacus* was injected into mice by means of a similar technique In both sets of animals the death time was measured Heparin did not affect the toxicity of either venom, but prolonged the death time in heparinized animals The authors point out that "in Australian snake venoms there appear to be three distinct principles, namely, formation of lysolecithin, a thrombotic and a neurotoxic principle" They suggest that these three elements may act at separate times, the thrombotic and lysolecithin effects acting first Heparinization might inhibit the thrombotic effect and allow the more slowly acting neurotoxic principle to kill, so lengthening death time Alternatively, the three elements of the venom might act together, the heparin, by minimizing one of them, might extend the period of life After doses near the LD<sub>50</sub> heparin did not allow survival but merely prolonged life The authors suggest that heparin might be useful therapeutically in that the life of persons suffering from black-snake or tiger-snake bite might be prolonged by its administration so that other forms of treatment of known value might be given more opportunity to act B G Macgregor

VACHON M Etudes sur les scorpions Chapitre III Description des scorpions du Nord de l'Afrique (Maroc Algérie, Tunisie Sahara algérien et Fezzan) [Studies on Scorpions III Descriptions of North African Scorpions] *Arch Inst Pasteur d'Algérie* 1948 June v 26 No 2, 162-208 figs 87-147

EARLE K V Injuries produced by Tropical "Water-Beetles" *Trans Roy Soc Trop Med & Hyg* 1948, July, v 42, No 1, 101-4, 2 figs [10 refs]

In Ecuador three species of water-beetles are found *Lethocerus campost* up to 3½ inches in length, *L. annulipes*, to 2½ inches, and *Belostoma boops*, to 1 inch They live on aquatic insects, fish and frogs, and may attack and kill birds They are attracted by bright lights and in the rainy season may leave the ponds sewers and marshes for the land and are found congregated at the base of lamp-posts They do not as a rule bite man unless handled The bite of the largest is painful and causes at first blanching, then swelling, redness

and throbbing these usually clear up in 24 hours but occasionally cellulitis and abscess follow. Treatment is symptomatic ammonia locally in the early stages later if there is suppuration, sulphonamides or penicillin. The existence of poison glands is uncertain there are two pairs of glands lying lengthwise along the oesophagus and, just above the beak, the cephalic glands, the homologues of the maxillary glands. Whether any of these produces venom has yet to be determined. The ventral and dorsal aspects of the largest water beetle the first named, are well reproduced in two photographs.

H. Harold Scott

## DERMATOLOGY AND FUNGUS DISEASES

AGUIRRE PEQUEÑO E. & GONZALEZ, R. E. Mal del pinto. (Bibliografía)  
[Bibliography of Pinta.] *Medicina, Mexico*. 1948, July 10 v. 28, No. 559  
— 57-313

This immense compilation occupies more than 50 pages and is evidence of very great industry and patience. After a brief introduction, the authors give a lengthy list of synonyms for this disease, shown topographically for different American countries. The bibliography is then presented in alphabetical order of authors and this occupies 18 pages a chronological bibliography from the year 1525 to 1948 takes another 18 pages then follow bibliographies relating respectively to geographical distribution, aetiology epidemiology inoculation experiments possible vectors, clinical features, pathology differential diagnosis, serology and treatment. Further short bibliographical references deal with historical work monographs, theses, general papers books and commentaries the last named includes references to *Pinta* in this *Bulletin* from 1913 to 1946. The very large number of contributions to the literature by the senior author himself is additional evidence of his wide knowledge and experience of his subject.

This paper constitutes a very useful compendium of the literature of pinta.

H. J. O. D. Darke-Gaffney

DELAMATER, E. D. Technique and Identification of Fungi of Medical Interest.  
*Amer. J. Clin. Path.* 1948, Mar. v. 18, No. 3, 233-48, 3 figs. [13 refs.]  
[Summary appears also in *Bulletin of Hygiene*]

The pathogenic fungi which may occur in various human materials are tabulated and methods for direct observation and culture are briefly described. The indiscriminate use of the so-called 'abouraud' medium is criticised. Though this medium is suitable for primary isolation of the dermal phytes and of *Candida* the use of cornmeal agar dextrose nutrient agar blood agar and thioglycollate broth for other fungi is described. Bacterial contaminant may be prevented by penicillin-tryptocyclin medium but it is not possible to inhibit the growth of saprophytic fungi. The mouse is a valuable diagnostic animal for routine use and, while it may be essential in the isolation of *Sporothrix* and *C. immitis* is useful also in determining the diagnosis of infections by other fungi.

The paper concludes with a short description of each of the important disease-producing fungi and is illustrated by 3 plates. The author states that actual culture and confirmation of the dermal phytes is not essential to all the diagnosis of the treatment of the fungus infections and that the Campbell method used by C. Cant and others for the identification of *Candida* with an agar diffusion test is far more reliable than the old method.

stimulated by minute budding cells of *Candida albicans* in smears The differentiation of *Actinomyces bovis* from *Nocardia asteroides* is clinically important in view of their different drug sensitivities R W Riddell

BOURGAIN, M & BAZIL, A Onychomycose à favotrichophyton d'origine exotique Coexistence de deux jordanons de type achorion [Tropical Favus of the Nails Co-existence of Two Jordanons of Achorion] Rev Méd Nav (Métropole et Outre-Mer) Paris 1948, v 3, No 2, 185-8

Brief clinical details are given of a case at Cherbourg of favus of the nails in a ship's electrician who had developed this rare condition abroad The causal fungus was obtained in culture in two forms which were considered to correspond with *Achorion brumptii* and *A. mulochevitchii* of LANGERON and BAEZA [see this Bulletin, 1937, v 34, 178], two jordanons [near species] of A [Trichophyton] G C Ainsworth

DE MEIRA, M. T. V., SIMÕES, T. S. & NOGUEIRA, J. F. P. Sobre a existência do "pé musgoso" na Ilha de S Nicolau (Cabo Verde) [The Presence of "Mossy Foot" in S Nicolau, Cape Verde Islands] An Inst Med Trop, Lisbon 1947, Dec, v 4, 269-79, 9 figs on 4 pls

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NEGRONI P & RADICE J C La formación de endosporos en el coccidioides munitis observado con la luz de Wood Su posición sistemática [The Formation of Endospores in *Coccidioides munitis* observed with Wood's Light The Systematic Position] Rev Argentina Dermatofilologia 1947, July-Dec, v 31, Nos 3/4, 573-8 3 figs [21 refs] French summary

SNYDER, B. L. & ROGERS, G. K. Disseminated Coccidioidal Granuloma (Case Report) Arizona Med 1948, Mar, v 5, No 2, 33-7

The disseminated form of infection by *Coccidioides munitis*, which carries a mortality rate of more than 50 per cent, constitutes only 0.2 per cent of all cases of coccidioidomycosis The primary, or pulmonary, form is prevalent in Arizona and is usually non-fatal

The case history is described of the disseminated disease in a young adult white male who had resided in Arizona for 3 years He complained of fatigue, cough, fevers, muscular aches and loss of weight, and examination revealed an upper lobe pulmonary lesion Three months later cutaneous coccidioidomycosis had developed over the chest and face and grew progressively worse The coccidioidin test and specific serological reactions were negative Raised intracranial pressure led to death of the patient about one year after his initial hospital attendance The cerebrospinal fluid had shown an increase in protein and lymphocytes, but culture was negative

A wide distribution of coccidioidal granulomata was demonstrated at necropsy, the liver was not obviously involved Cerebrospinal lesions were limited to the meninges, where fungus spherules tended to be larger and more actively proliferating than elsewhere The clinical and pathological features of the cutaneous disease are discussed

R W Riddell

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H. J. O'D. Burke-Gaffney

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## TROPICAL ULCER

D ALMEIDA, J. Sept cas de cancrs graves sur ulcères phagédéniques à l'Hôpital Central en 1948. [Seven Cases of Cancer Superimposed on Tropical Ulcers in the Central Hospital in 1948.] *Bull. Méd. de l'Aspe Oculistique Française*, 1947, 4 No. 2, 99-102.

HARR, J. Studies in Tropical Ulcer. Part I. The Origin of an Epidemic. *J. Trop. Med. & Hyg.* 1948, Mar. v. 51 No. 3 47-53 4 figs. (7 refs.) Part II. The Aetiology of Tropical Ulcer *Ibid.* Apr., No. 4 7-81 (18 refs.) Part III. The Insect Vector *Ibid.* May, No. 5 99-102. (12 refs.) Part IV. The Treatment of Tropical Ulcer *Ibid.* June No. 6 119-28. (23 refs.)

I. In this paper the term 'tropical ulcer' is reserved for acute ulcers having a phagadaemic tendency and which are characterized clinically by a foul smell and an adherent slough overlying a soft granulomatous base that bleeds easily. Bacteriologically, the fusiform bacillus is constantly found whatever other organisms may be present.

The Tingri district in Assam, in which the work reported was carried out covers an area of about 144 square miles, and is almost absolutely flat, the soil being the usual alluvial silt of the Brahmaputra valley. In it are found 201 estates, areas of forest and scrub jungle, rice land, and scattered native villages. The population consists chiefly of aboriginals from Central India with some Nepalese and Assamese in the villages. November to February are dry and comparatively cold, March and April are warmer with scattered rainfall, and May to October hot and humid with a fairly high rainfall. The average yearly rainfall is about 95 in., of which about 25 in. fall during the latter period. Shade temperatures are not above 100 F. but humidity percentages of 90 and over are common.

Up to 1941 tropical ulcer was very rare in this district. About 1941 hundreds of labourers were sent to the outfields for jungle clearing and to various military works.

The author gives a table of the incidence of the disease in 13 estates on which he worked. Out of a total estate population of 20,000 1101 cases (5.52 per cent.) were met with but the condition was also widespread in the neighbouring villages. From a study of the incidence on tea estates it was noticed that an appreciable period elapsed between the appearance of the disease in one line and its spread to another. Study of the figures for 13 estates in each month of 1948 showed that during the 4 cold dry months (November to February) the incidence was nil. There was thus for no carry-over of cases from one season to the next and maintenance of the infection cannot be blamed on isolated sporadic cases during the cold months. All author uses appear to agree that natural or acquired immunity does not occur in tropical ulcer.

The paper is illustrated with five tables and four figures and the tables include figures for the incidence of tropical ulcer from 1947 to 1948 inclusive.

II. The author considers that (1) Tropical ulcer is a specific disease caused by infection by the fusiform bacillus. Under ordinary conditions only man is susceptible; experimental infection of the ordinary laboratory animal having been found impossible. One observer however states that the Nigerian hedgehog is susceptible (SMITH, T. & R. & S. *J. P. Med. & Hyg.* 1943 v. 48 259). There is no evidence that a filterable virus is responsible (this *Bull.* 1946 v. 49 58).

(2) The condition is confined to warm countries and to seasons of moderate heat and rainfall. The disease disappears under conditions of extreme heat and drought, and excessive wetness and rainfall.



## Tropical Ulcer

Vol 45, No 11]

(3) Tropical ulcer can be maintained in a population without any carry-over of cases from one season to the next. As the causal bacillus is difficult to culture and is easily destroyed, it is unlikely that infected fomites or dust carry the infection, and there is no evidence that it is harboured by animals. The human mouth is probably not an important agent in carrying the infection, and is certainly not an important factor in its dissemination.

(4) Infection is confined almost entirely to adults and older children, but the type of work being done is not of primary importance. The disease is one of rural or semi-rural living conditions, but needs a reasonable density of population for its spread.

(5) Although some degree of trauma probably always precedes the appearance of an ulcer, this may be very slight.

(6) In an area where tropical ulcers are prevalent, certain sub-areas are much more heavily infected than others.

(7) There is no definite evidence that tropical ulcer is a deficiency disease, and neither malaria nor alcoholism appears to play any important part in its causation.

(8) The majority of tropical ulcers appear on a limited area of the body, but it is very doubtful whether the explanation advanced that this area is one of deficient blood supply is correct.

(9) The seasonal character of the disease and its predilection for one particular class and for certain geographical areas suggest that the infection is carried and harboured by an insect vector. The limited portion of the body normally affected suggests that this vector is a crawling insect.

III For many years in Assam it has been the opinion of medical men, especially those working on tea estates, that tropical ulcer is an insect-borne disease. This has been more a matter of conjecture than the result of a close study of epidemiology, the most widely held view being that abrasions are infected by various flies which have previously settled on existing ulcers and act merely as mechanical transmitters. The eye-fly (*Siphunculina fomicola*) has been incriminated, mainly owing to its close seasonal incidence with the disease. In only one case did a medical man succeed in infecting himself by allowing one of these insects to feed on a typical ulcer and then transferring it to an abrasion on his own body. Subsequent observers were uniformly unsuccessful, and moreover the disease is frequent in districts where the fly is unknown.

The average estate labourer's house is full of such insects as the cockroach, bed bug, louse flea sandfly, and housefly. These are more likely to attack children than adults but it is known that the former are rarely affected. Adults usually defaecate in some patch of scrub jungle not far from their houses, passing through moderately long grass on the way. Children under the age of 6 usually defaecate in the close vicinity of their houses on bare earth, and the older ones up to 12 on the roads adjacent to the coolie lines. There is thus a marked correlation between the sanitary habits of the various age groups and the incidence of the disease.

Outdoor winged insects bite any part of the body indiscriminately and, other things being equal, if these were incriminated it would be expected that tropical ulcer would appear anywhere on the body, but in fact over 95 per cent of cases are confined to the leg, ankle, and dorsum of the foot.

The argument is put forward that the vector is a crawling insect which lives mostly in jungle or coarse vegetation and can retain an infection from one year to another. Ticks and mites are the insects which best fulfil these requirements, and are probably found in all countries where tropical ulcer is known. It has been established that they are capable of retaining certain infections from year to year. If the hypothesis is accepted that a tick or mite is the vector, the

## TROPICAL ULCER

D ALMEIDA, J. Sept cas de cancers greffés sur ulcères phagédéniques à l'Hôpital Central en 1946. [Seven Cases of Cancer Superimposed on Tropical Ulcers in the Central Hospital in 1946.] *Bull. Méd. de l'Asy. Occidentale Française* 1947 v 4 No. 2, 103-103.

HARR, K. Studies in Tropical Ulcer. Part I. The Origin of an Epidemic. *J. Trop. Med. & Hyg.* 1948 Mar v 51 No. 3, 47-53, 4 figs. [7 refs.] Part II. The Aetiology of Tropical Ulcer. *Ibid.* Apr No. 4, 77-81 [18 refs.] Part III. The Insect Vector. *Ibid.* May No. 5, 99-103. [12 refs.] Part IV. The Treatment of Tropical Ulcer. *Ibid.* June No. 6, 119-28. [28 refs.]

I. In this paper the term "tropical ulcer" is reserved for acute ulcers having a phagadaemic tendency and which are characterized clinically by a foul smell and an adherent slough overlying a soft granulomatous base that bleeds easily. Bacteriologically, the fusiform bacillus is constantly found whatever other organisms may be present.

The Tingri district in Assam, in which the work reported was carried out covers an area of about 144 square miles, and is almost absolutely flat the soil being the usual alluvial silt of the Brahmaputra valley. In it are found 20 tea estates, areas of forest and scrub jungle, rice land, and scattered native villages. The population consists chiefly of aborigines from Central India with some Nepalese and Assamese in the villages. November to February are dry and comparatively cold, March and April are warmer with scattered rainfall and May to October hot and humid with a fairly high rainfall. The average yearly rainfall is about 95 in. of which about 85 in. fall during the latter period. Shade temperatures are not above 100 F. but humidity percentages of 90 and over are common.

Up to 1941 tropical ulcer was very rare in this district. About 1941, 400 of labourers were sent to the oilfields for jungle clearing, and to various military works.

The author gives a table of the incidence of the disease in 1948 in 13 estates on which he worked. Out of a total estate population of 31,849 1101 cases (5.32 per cent.) were met with but the condition was also widespread in the neighbouring villages. From a study of the incidence on tea estates it was noticed that an appreciable period elapsed between the appearance of the disease in one line and its spread to another. Study of the figures for 13 estates in each month of 1948 showed that during the 4 cold dry months (November to February) the incidence was nil. There was therefore no carry-over of cases from one season to the next and maintenance of the infection cannot be blamed on isolated sporadic cases during the cold months. All authorities appear to agree that natural or acquired immunity does not occur in tropical ulcer.

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almost universal finding of ulcers below the knee is capable of a simple mechanical explanation namely as a man walks through long grass or brush most of the insects attaching themselves to the foot are brushed off but any above the ankle tend to remain there. Further the leucocytic infiltration into the base of the ulcer consists largely of eosinophiles, and this has been found to be very characteristic of lesions caused by the bites of harvest mites and various species of ticks. Again ulcers are most frequent among the strongest labourers, these being the people who go most into the jungle to cut firewood and hunt game.

IV The results of various methods of treatment and the literature on the subject are reviewed very fully.

The author describes the treatment of 483 cases, all being of the typical acute type. In 184 instances more than one ulcer was present, the number varying from two to eleven, while in this series both legs were affected in about one-third of cases.

Eight different methods of treatment were tried and are described in detail. The criterion of cure was firm and complete healing, in 47 days and the following routine treatment was found to be most satisfactory. After preliminary cleansing with sterile normal saline the ulcer is dressed twice daily for five days with sterile gauze moistened with a solution of 500 units of penicillin per ml. On the first day of treatment 100,000 units of penicillin are given intramuscularly in five three-hourly injections. From the sixth day onward, the ulcer is dressed daily with scarlet-red ointment but at the slightest sign of the sore becoming foul again the local penicillin dressing is repeated for three or four days. If serious reinfection has occurred it is advisable to repeat the parenteral administration of penicillin but each case should be treated on its merits. No difference was apparent in giving more than 100,000 units in any one course and the value of this drug is particularly apparent in ulcers over 1 inch in diameter. In the case of the larger ulcers skin grafting helps to reduce the time required for epithelialization.

One difficulty of penicillin treatment is that some form of refrigerator is necessary unless very large numbers of patients are being dealt with, when the whole contents of one phial can be used immediately it has been dissolved, as otherwise there will be much wastage. In the absence of penicillin the smaller ulcers can best be treated with the copper sulphate phenol and glycerin jute method, followed by a choice of cod liver oil, acacia or emulsion or scarlet-red ointment (thus *Bulletin* 1938, v 35 828). The author apparently does not use surgical debridement. Of 128 cases treated by penicillin, 79.7 per cent. were regarded as successes with single ulcers of 1 inch or more in diameter 84.2% successful. [For descriptions of the comparative methods of treatment tested, the original paper should be consulted.] C F Skellern

### MISCELLANEOUS DISEASES

CHALGLEY W. S. & BAKER A. B. The Nervous System in Tropical Disease. A Clinical Review. *J. Clin. Med.* 1947 Dec. 20 No 4 385-439 407 (a).

This paper is a review and not suitable for abstraction. It should be referred to in the original by those particularly interested in the diseases discussed, namely yellow fever dengue epidemic and endemic typhus Rocky Mountain spotted fever tinea, amebic disease Q fever bartonellosis bacillary dysentery cholera plague melioidosis leprosy malaria African trypanosomiasis South American trypanosomiasis leishmaniasis relapsing fever rat bite fever acariasis ascariasis hookworm infection filariasis schistosomiasis and 12% continue.

In each case a thumb-nail sketch is given of the disease as a whole and this is followed by a review of references to "neuropsychiatric manifestations and complications" that have appeared in the literature. The subject, however, is treated mainly from the point of view of the organic neurologist and, for example, the well-known neuropsychiatric manifestations associated with filariasis (Bancroft's) are not discussed.

Naturally, the sections vary in length: there are for example 54 references in the malaria section, most of which are of recent date, whereas the author has only been able to muster 4 for Bancroft's filariasis and they are all 20 or more years old; three of these refer to the finding of microfilaria in the blood vessels of the brain, and only one, an unimportant one, suggests that there are any associated symptoms.

The paper is a very laborious piece of work

L E Napier

## PROTOZOOLOGY GENERAL

WARREN, J & RUSS, Sudie B. Cultivation of *Toxoplasma* in Embryonated Egg An Antigen derived from Chorioallantoic Membrane. *Proc Soc Exper Biol & Med* 1948, Jan, v 67, No 1, 85-9, 1 fig

By means of toxoplasma-infected chorio-allantoic membranes from infected chicken eggs complement-fixing antigen was prepared. The membranes were ground in a mortar with alundum and a 10 per cent suspension was prepared in physiological saline buffered at pH 7.4. The crude suspension was frozen and thawed three times and clarified by 15 minutes' centrifugation at 3,500 r.p.m. The supernatant fluid, after the addition of merthiolate to 1:10,000, constituted the antigen. This was generally stored at  $-20^{\circ}\text{C}$ . An antigen for use as control material was prepared in the same way from normal 16-day-old chick embryos. Sera were obtained from rhesus monkeys and guinea-pigs convalescing from a toxoplasma infection and from a number of patients suspected of suffering from toxoplasma infection. The fixation tests were performed as follows:—In tubes were placed 0.25 cc of the dilution of serum, 0.25 cc of the antigen and 0.5 cc of fresh diluted guinea-pig serum containing two units of complement. They were incubated at  $5^{\circ}\text{C}$  overnight. The haemolytic system, consisting of 0.5 cc of a mixture of equal parts of 3 per cent suspension of washed sheep erythrocytes in saline and diluted amboceptor (2 units) was added to the tubes. They were incubated at  $37^{\circ}\text{C}$  for half an hour and read in the usual manner. The immune animal sera were positive (1 in 200 to 400) as also were human sera from both proven and suspected cases of toxoplasmosis (1 in 16 to 128).

C M Wenyon

MACFARLANE, J O & RUCHMAN, I. Cultivation of *Toxoplasma* in the developing Chick Embryo. *Proc Soc Exper Biol & Med* 1948, Jan, v 67, No 1, 1-4, 2 figs

Inoculation of toxoplasma—the "R.H." strain of SABIN—in the yolk sac of chicken eggs of 7 to 11 days' incubation resulted in the death of the chicken embryo on the 5th to the 6th day. Examination of the eggs showed numerous yellow-white plaques, 0.5-3 mm in diameter, on the chorio-allantoic and amniotic membranes. The areas surrounding the lesions were thickened and histologically represented regions of dense cellular infiltration containing numerous toxoplasma. Smears of the membranes revealed numerous toxoplasma, which were also present in the organs of the embryo. Inoculation of the parasites into mice, rats, chicks, rabbits and rhesus monkeys

produced infections which did not vary from those produced by inoculation of the original strain from the mouse. The passage through the chick embryo did not modify the parasite in any way. Attempts to cultivate the toxoplasma in the pooled embryonic fluid from 17-day fertile eggs were unsuccessful. Storage of infected membranes at 4 C. yielded viable organisms up to one month. Photographs illustrate the appearance of the normal and infected chorio-allantoic membrane and the difference between microscopic sections of these.

C. M. HENYON

WISSER J. VERLINDE J. D. VAN TRIEL, P. H. DAVEL, J. & VAN DER ELST P.  
Isolation of *Toxoplasma* from Cerebrospinal Fluid of a Living Infant in Holland. *Pro. Soc. Exper. Biol. & Med.* 1948 Mar v. 67 No. 3 29-4

The diagnosis of toxoplasmosis is frequently made on the evidence of serological reactions and the presence of ocular changes in the patient. Final confirmation by demonstration of the organisms is much less frequent and seldom achieved, as it was in the case under review during life.

The patient, a child six weeks old on admission to hospital, appeared healthy during the first few weeks of life. When first seen in hospital he presented marked ocular changes, displacement and enlargement of the lateral ventricles and developing hydrocephalus.

The centrifuged deposit of the cerebrospinal fluid, when examined microscopically, showed numerous toxoplasma bodies. The cerebrospinal fluid, inoculated intracerebrally into mice produced infections in the latter.

The serum of the child's mother showed strong neutralizing power against the organism when examined by Sabin's rabbit skin test. Cross immunity tests for neutralizing activity between the organism isolated and another human strain from America showed that the two strains were very closely related, if not identical.

H. E. SHAW

## ENTOMOLOGY AND INSECTICIDES GENERAL

CALLOT J. La réaction de l'homme aux piqûres de moustiques. [Man's Reaction to Mosquito Bites.] in *L'Asiat. H. malaise et Comparée* 1947 v. 22, Nos. 3-4 233-4

The author refers to the notes on the subject by MELLANBY (ibid. *Bunch* 1947 v. 44 40 and 364) by BRISTOWE and by RIBBANS (ibid. 364) and in general confirms their conclusions on relative attractiveness or otherwise of different persons to mosquitoes.

In his experience with *A. des aegypti* however, a person who is re-bitten continuously by the mosquito after an interval of several months presents a delayed reaction (Mellany Stage I) after another interruption of 1-10 days followed by a new series of bites he passes directly into Stage III and thus state periods for three months elapse daily bites.

On the other hand, experiment with *Culex at. ku* Ribbans showed that the reaction produced in this case after the initial bite was that of stage II without Stage I having been entered at all.

The author has never succeeded in obtaining stage IV experimentally. He suggests that some people attain it, while others are free from any reaction from the outset. He draws a distinction between those who have never been bitten by mosquitoes and those who do not react to the bite and gives an example of a subject who had never been in contact with *A. des aegypti* but suffered no reaction whatever when he was bitten experimentally by this species.

H. J. O'D. BURKE & J. J. J. J.

ABBOTT, P H The Culiidae (Diptera) of Darfur Province, Anglo-Egyptian Sudan, with Observations on the Geography and Zoogeographical Relations of the Region *Proc Roy Entom Soc London* Ser B 1948, Apr 26, v 17, Pts 3/4, 37-48, 1 map [10 refs]

Darfur is the most westerly province in the Sudan It lies at the northern limit of the Ethiopian region and includes the Marra mountains rising to over 10,000 feet

The topography and climate are described and notes are given on the distribution and breeding places of the mosquitoes The majority of the mosquito records were made in the dry season [year not stated] as travel is almost impossible in the wet season Nine species of *Anopheles* and twenty-seven culicines were collected *A. gambiae* is the commonest anopheline and the only malaria vector in the area Other mosquitoes whose presence in Darfur is of particular interest are *Anopheles ruficollis* and *Aedes arabiensis*, not previously found so far west as this, *Culex latincinctus*, known from Arabia, E Africa and the Mediterranean region, and *Culex grahami*, previously known only in the west, southern Congo and Uganda *Aedes aegypti* was widely distributed in the province  
H S Leeson

DE MEILLON, B New Records and Species of Biting Insects from the Ethiopian Region II Reprinted from *J Entom Soc South Africa* 1947, Aug 30, v 10, 110-24, 4 figs

The new species described in this paper include a mosquito *Anopheles mascarensis* male and female from Madagascar, two Ceratopogonidae, *Culicoides acastus* male and *Alluaudomyia transvaalensis* female, both from the Transvaal and the males and females of five fleas, from various parts of Southern Africa, *Xenopsylla pastphae*, *X. mulleri*, *X. achilla*, *X. bechuananae* and *Chasitopsylla capensis* A list is given of 12 Anopheline and 22 Culicine mosquitoes collected in Bechuanaland  
H S Leeson

LICHTENSTEIN E P Growth of *Culex molestus* under Sterile Conditions [Correspondence] *Nature* 1948, Aug 7 227

STAGE H H A Vespilid preying on Anophellines *Mosquito News* 1948 June, v 8 No 2, 73

FAY, R W, COLE, E L & SIMMONS, S W Toxicity of DDT Residues Effect of Surface and Surface Treatment on the Residual Toxicity of DDT against Adult *Anopheles quadrimaculatus* Mosquitoes *Soap* New York 1948, June, v 24 No 6, 130-33, 157-9, 189, 3 figs

These experiments constitute an extension of earlier work and the same technique was employed [see CLAPP, FAY and SIMMONS, this *Bulletin*, 1947, v 44, 563, SIMMONS *et al*, *ibid*, 1946, v 43, 789, FAY, SIMMONS and CLAPP, *ibid*, 1947, v 44, 562] In brief, adults of *Anopheles quadrimaculatus* were exposed for sixty minutes in a small box, the sides of which are made up of various materials (in different tests) and treated with DDT at the rate of 200 mgm per sq ft The surfaces investigated were, plain pine plywood (standard), dry bamboo, rusty metal screen, rusty sheet metal, bark, new sheet metal, glass, tile, palmetto thatch, new metal screen, "plexiglass", shellacked wood, synthetic fabric, cement and waxed wood DDT was sprayed on as a xylene-Triton X emulsion, as a kerosene solution or as an aqueous suspension

The results indicated a better persistent toxicity (up to forty-five weeks) on relatively rough surfaces (rusty metals, bark) "which might be expected to aid

produced infections which did not vary from those produced by inoculation of the original strain from the mouse. The passage through the chick embryo did not modify the parasite in any way. Attempts to cultivate the toxoplasma in the pooled embryonic fluid from 17-day fertile eggs were unsuccessful. Storage of infected membranes at 4°C. yielded viable organisms up to one month. Photographs illustrate the appearance of the normal and infected chorio-allantoic membrane and the difference between macroscopic sections of these.

C. M. H. 1948

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H. E. Short

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H. J. O'D. Burke-Gibney



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spray coverage and adherence." Smooth but impermeable surfaces were next in order of efficiency, and least satisfactory were either waxed or shellacked surfaces (which might have softened and absorbed DDT) or else very porous materials (cement).

These results were true, generally speaking, of treatments with emulsion and kerosene solution. The suspension of the DDT wettable powder was definitely better on the absorbent cement and somewhat better on the new metal and glass; it gave inferior results on the rough surfaces of rusty metal and bark.

Various household cleansing measures were tested for their effects in reducing residual toxicity of DDT films. With fabrics, dry cleaning was most drastic, followed by vigorous brushing and (least serious) vacuum cleaning. DDT was removed from walls by periodic dusting, and more rapidly if a past cleaner was employed.

J. R. D. 1948

RAFFAELLI D. Determinazione colorimetrica del DDT sullintonaco delle pareti trattate. (Colorimetric Estimation of DDT on Treated Walls.) *Riv. di Parassit.* Rome. 1948, June 1, 9 No. 1, 79-83. English summary (2 lines)

The following method, derived from Chalkin's reaction (*Ind. Eng. Chem., Analytical Ed.* 1948 v. 18, 279) is useful for rapid estimation of DDT present on walls and other surfaces sprayed for residual insecticidal effect.

The superficial layer of surface is scraped from 100 sq. cm. on to a piece of paper and thence transferred to a test tube. The DDT is extracted with about 4-5 ml. of ether which is decanted into another tube. This tube is placed on a water bath and the extract is evaporated to dryness. To the residue 2 ml. of glacial acetic acid are added and the tube is warmed for a short time on the bath with agitation, then 10 ml. of sulphuric acid (D 1-84) are added and the mixture is heated on the bath for ten minutes.

The presence of DDT is indicated by a yellowish colour with a tinge of green, the depth of colour indicating the amount of DDT present. For quantitative work standards are made up with 0.5 to 5 milligrammes of DDT. The colours produced in this reaction are then matched by dilutions of a solution of Grubler meta chrome yellow. R.D. to which a trace of Grubler methyl green has been added. These solutions are kept as reference standards.

This method is accurate if the DDT application has been made with kerosene solution. When an emulsion or dispersion has been employed, there may be traces of emulsifying or dispersing agents which introduce a brownish tinge, sufficient to interfere with a quantitative determination. This can be avoided as follows. The deposit from the ether extract is treated with a few ml. of concentrated potassium permanganate and placed on the water bath to evaporate to dryness. A new ether extraction is then made and the test conducted in the usual way.

J. R. D. 1948

SCOTT J. A. An Apparatus for removing Tropical Rat Mites from Large Quantities of Bedding Materials. *J. Parasitology* 1948 34 31 3p. 2, 132-3 1 fig.

This apparatus was constructed for the purpose of extracting within a single working day large numbers of adult and nymphal tropical rat mites (*Liponyssus bacchi*) from about 4,000 cc. of wood shavings and an equal charge of hay. It consists of an open trough of galvanized sheet iron (2 ft 8 in. x 8 in. x 4 in. deep) surrounded by moist containing water maintained at a depth of 1 in. An infra-red bulb of 250 watts is provided over the trough moves along at the rate of 1 in. per hour. The mites are driven ahead of the waves of heat and are

collected by means of a suction bottle. The bottom of the trough is lined with asbestos cement to delay heat conduction and prevent mites being killed when they drop off the ends of pieces of hay. A line drawing illustrates the apparatus and gives all necessary dimensions, it also shows a simple device for collecting mites which fall into the water in the moat. *H. S. Leeson*

## REPORTS, SURVEYS AND MISCELLANEOUS PAPERS

SERGEANT Ed Le Professeur Félix Mesnil Zoologiste et Chef d'Ecole en Médecine coloniale [Professor Felix Mesnil, Zoologist and Chief of the Colonial School of Medicine] Reprinted from *Rev de la Méditerranée* 1948, v 5, 24 pp

DUBOIS, A & DUREN, A Soixante ans d'organisation médicale au Congo Belge [Sixty Years of Medical Organization in the Belgian Congo] *Liber Jubilæis J Rodham (Soc Belge Méd Trop, Brussels)* 1947, Dec, 1-36 [19 refs]

This contribution to the *Liber Jubilæis J Rodham* contains an account of the development of the medical services of the Belgian Congo, with which, from 1903 to 1925, Rodham was so closely associated, he was the head of that service for five years. The service has grown from small beginnings, and as a result of special needs it has developed in various directions. For instance, the heavy incidence of sleeping sickness led to the development of a special section, which in turn has been expanded into the *Service d'Assistance Médicale Indigène* and finally into the Foréamu service.

Training in medicine is given on a large scale to African auxiliaries and to the various subordinate grades, and schools for these purposes exist in nine cities. The government assumes responsibility for the health of the community, but encourages private initiative, for instance the Red Cross and university foundations, religious missions and the medical services of the big industries. In 1944 there were 176 physicians in government and Foréamu service, 127 in other organizations, 15 private practitioners, and large numbers of *infirmières* and *agents sanitaires* [whose status is not here defined].

Scientific research in the Congo has a distinguished history, and there are now laboratories at 5 government stations and at various mines and Red Cross institutions. Scientific missions have played a great part in medical development, and continue to do so.

Of the important diseases, malaria is mentioned first. For trypanosomiasis the index of infection has fallen from 1.1 in 1927-29 to 0.23 in 1946 (3½ million examined in 1946). Schistosomiasis (mostly intestinal) is fairly common in the south and east, where *Planorbis adowensis* and *P salinarum* are the snails. Vesical schistosomiasis does exist, however, and *Physopsis africana* is the host. The dysenteries, relapsing fever, leprosy (58,830 cases known), venereal diseases, cerebrospinal fever, yaws (quarter of a million treated each month, permanently affecting 2-3 per cent of the population), tuberculosis, plague, yellow fever, smallpox and murine typhus, are all important. Some of them are rather potential than actual sources of widespread danger, but all need, and receive, considerable attention.

The article is an interesting conspectus of the present situation.

*Charles Wilcocks*

Sorzi, M. Relazione Triennale (1945-1947) sull'attività del Laboratorio. [The Work of the (Entrea) Laboratory for the Period 1945-47] *Bull. Soc. Ital. di Med. e Ig. Trop.* (Sez. Entrea) 1948, v. 8, No. 12, 31-53. [19 refs.]

The Laboratory of Hygiene and Prophylaxis of Entrea has become also the Central Laboratory of Pathology and, with a staff comprising a director an assistant 6 technicians, an administrator a registrar and 4 laboratory boys (*aiuti di servizio*) it deals with 100-120 specimens a day. For purposes of this report the work has been divided into five sections:

(1) *Biochemical* dealing with 27,180 specimens during the period, including examinations of urines, gastric contents, cerebrospinal fluids, blood samples and sputa not easily separated from

(2) *General microscopic and parasitological* Search for intestinal protozoal and helminthic infestations, differential blood counts and blood parasites malaria plasmodia and sporozoites.

(3) *Serological* including 36,320 Wassermann reactions 5,036 Widal-Felix tests and preparation of antisera for precipitin reactions blood grouping, etc. In an outbreak of typhus in Asmara in 1946-47 *Proteus O119 O1*, and *O1A* were used. Reactions to the first named were much the most numerous. Of 100 "nationals" (presumably Italians) 44 so reacted in a dilution of 1:1280 5 to *Proteus O1*, while of 1,000 indigenes the respective figures were 32.3 and 8.1 per cent.

(4) *Histological* and (5) *Bacteriological*

An anti-rabies dispensary has been joined to the laboratory where the vaccine is prepared and treatment given. The author states that undulant fever due to *Br. melitensis* and *paratuberculosis* is a disease of the towns. *Br. abortus* infection, he avers, does not occur. Bacillary dysentery is apparently uncommon during the three years 350 samples of faeces have been cultivated and the *Shigella* faecal organism has been isolated on 6 occasions, a Flexner organism 4 times and a Sagon strain once. Amoebic dysentery is more common, but not above 15-20 per cent. [the number examined is not however stated] and has become more widespread during and after the war years.

H. Harold Sefton

SOUTH PACIFIC BOARD OF HEALTH. Minutes of the Meeting held at Suva, Fiji, on the 25th, 28th and 31st October 1946 [BUCHANAN J. C. R. Chairman] 8 pp. Fiji Govt. Press.

At the inaugural meeting of the South Pacific Board of Health many subjects relating to that area were discussed. The Chairman Dr J. C. R. Buchanan, who holds the dual office of Inspector General South Pacific Health Service and Director of Medical Services Fiji, outlined the problems connected with health administration in the different islands and made it clear that the need was for integration which would include a domestic medicine, of pharmacological information.

The meeting discussed questions relating to establishment research diet and nutrition, epidemiology and training of staff. It is evident that the Board were fully alive to the nature of the problem facing them and felt the need to take whatever steps to deal with them that might be available in cooperation with neighbouring territories, large and small.

The establishment expenditure of the Service Headquarters and the estimates for 1945-46 are shown as appendices to the minutes.

H. J. O'D. Burke-Grey

South Celebes, the large island to the east of Java, has a homogeneous population of Malays, 4 million inhabitants, with a density varying from 2 to 200 per square kilometre. They are agriculturists. Its capital, Makassar, headquarters of the public health service, has a population of 180,000, with one physician for 7,000 inhabitants.

An interesting account is here given of the principal diseases of the territory. One might have expected a reference to the Celebes vibrio, an even stronger competitor because of its cholera, not dysentery, syndrome, for equality status with the so-called "true" cholera vibrio than the El Tor variety. Cholera is not mentioned among the diseases of the island. Malaria is the most important sickness, with a heavy mortality toll among infants and young children. In some districts 50 to 90 per cent of the school children have large spleens, while some 300,000 out of 850,000 inhabitants of endemic areas suffer from chronic malaria. Malaria is, however, of small importance in the town of Makassar. Yaws is once again receiving the attention of the physician. Each patient should receive 3 salvarsan injections and every physician gives monthly some 1,000 injections, in some cases up to 4,000. There is serious shortage of salvarsan. Other diseases mentioned are avitaminoses such as beriberi, hookworm, endemic goitre, leprosy, tuberculosis, rabies and mental diseases. Filariasis and trachoma are not much in evidence.

Mortality and birth statistics are not yet forthcoming. Venereal diseases are not troublesome in rural areas, but are increasing in Makassar.

IV F Harvey

BRITISH GUIANA, MOSQUITO CONTROL SERVICE MEDICAL DEPARTMENT  
 Annual Report for the Year ended 31st December 1947 [EDDEY, L G,  
 Deputy Director of Medical Services & Acting Chief Officer] 7 mimeo-  
 graphed pp

The Yellow Fever Service and the Malaria Research Service in British Guiana have now been amalgamated into the Mosquito Control Service, but the two sections for *Aedes* control and for DDT spray, are kept separate. The former comprises 82 and the latter 78 persons, and the office a staff of 4.

No *Aedes* were found during the year's searches, in Georgetown, Demerara River Estuary, Bartica etc., Mackenzie-Wismar, New Amsterdam, Berbice, or in trains. In these areas routine measures are taken against breeding, and 5 per cent DDT in kerosene is extensively used as a spray at an estimated dosage of 150 mgm DDT per square foot. All trains were re-sprayed during July and August.

Precautions against introduction of insects by air are taken by the authorities of the U.S. Air Base, and local British Guiana Airways aircraft are disinfested by the company. Inter-colonial schooners and government ships are sprayed with DDT from time to time with good results, and large ocean-going vessels, which are treated with DDT, are no longer sources of reinfestation.

Yellow fever immunity surveys were continued. 220 sera being examined at the Rockefeller Foundation Laboratory, Bogota Colombia, of these 34.1 per cent were positive for protective bodies. The specimens were mostly taken from people in the interior, and positive results were obtained in children; these findings indicate that jungle yellow fever still occurs to a considerable extent in the Aboriginal Indians.

SPONZA M. Relazione Triennale (1945-1947) sull'attività del Laboratorio. [The Work of the (Eritrea) Laboratory for the Period 1945-47] *Bol. Soc. Ital. di Med. e Ig. Trop. (Sez. Eritrea)* 1948, v. 8, No. 12, 31-53 [19 refs.]

The Laboratory of Hygiene and Prophylaxis of Eritrea has become also the Central Laboratory of Pathology and, with a staff comprising a director an assistant 6 technicians an administrator a registrar and 4 laboratory boys (*uomini di servizio*) it deals with 100-120 specimens a day. For purposes of this report the work has been divided into five sections:

(1) *Biochemical* dealing with 27-180 specimens during the period, including examinations of urines, gastric contents, cerebrospinal fluids, blood samples and suchlike not easily separated from.

(2) *General microscopic and parasitological*. Search for intestinal protozoal and helminthic infestations, differential blood counts and blood parasites: malaria plasmodia and sporochonts.

(3) *Serological* including 38,520 Wassermann reactions, 8,054 Weil-Felix tests and preparation of antisera for precipitation reactions, blood grouping, etc. In an outbreak of typhus in Asmara in 1946-47 *Proteus OX19 OX<sub>2</sub>* and *OXA* were used. Reactions to the first named were much the most numerous. Of 100 "nationals" (presumably Italians) 44 so reacted in a dilution of 1:1280. 5 to *Proteus OX<sub>2</sub>*, while of 1,000 indigenes the respective figures were 32.3 and 8.1 per cent.

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An anti-rabies dispensary has been joined to the laboratory where the vaccine is prepared and treatment given. The author states that nodular fever due to *Br. mediterraneus* and *paramediterraneus* is a disease of the towns. *Br. abortus* infection, however, does not occur. Bacterial dysentery is, apparently, uncommon during the three years 350 samples of faeces have been cultivated and the Shiga toxin organism has been isolated on 8 occasions, a Flexner organism 4 times and a Saigon strain once. Amoebic dysentery is more common, but not above 15-20 per cent. [The number examined is not by over stated] and has become more widespread during and after the war years.

H. Harold Scott

SOUTH PACIFIC BOARD OF HEALTH. Minutes of the Meeting held at Suva, Fiji, on the 25th, 28th and 31st October 1946 (Chairman: J. C. R. Buchanan) 6 pp. Fiji Govt. Press

At the inaugural meeting of the South Pacific Board of Health many subjects relating to that area were discussed. The Chairman, Dr J. C. R. Buchanan, who holds the dual office of Inspector General, South Pacific Health Service and Director of Medical Services, Fiji, outlined the problems connected with health administration in the different islands and made it clear that the need was for integration, which would include a domestic interchange of epidemiological information.

The meeting discussed questions relating to establishment, research, diet and nutrition, epidemiology and training of staff. It is evident that the Board were fully alive to the nature of the problems facing them and of the need to take whatever steps to deal with them that might be available in co-operation with neighbouring territories, large and small.

The establishment expenditure of the Service headquarters, and the estimates for 1945-46 are shown as appendices to the minutes.

H. J. O'D. Burke-Gaffney



No viscerotomy specimens were received during the year and no cases are reported from hospitals. Vaccination is carried out as required in Georgetown. Total general expenditure was 182,792 B.W. I. dollars. Charles Walcotts

Irons E. E. Report of the Medical Mission to Puerto Rico and to the Virgin Islands. *J Amer Med. Ass.* 1948 Apr 10 v 138, No. 13 979-84.

The author was a member of a medical mission of 8 eminent medical men and one woman (Director of a school of nursing in Chicago) who were invited by the U.S. Secretary of the Interior to report on medical conditions in Porto Rico and the Virgin Islands early in 1948. He reports his general impressions in this article which has considerable interest for medical administrators of tropical countries.

The greatest single factor in the health of the people of Porto Rico is that of nutrition—the total food supply locally produced and imported, is not enough for the population of over 2,000,000 which is increasing by 65 000 each year. Some improvement may come from development in the use of fruits like mangoes and guavas, at present little used and of fish, but that improvement cannot be great. It has been suggested that emigration would keep the population within reasonable limits, but this would need to involve over 50 000 each year. Increase in industrialization on present lines cannot cope with more than part of the problem. The net reproduction index of Porto Rico is 1.7 the highest in the world, and the 77 birth control clinics have so far had no demonstrable influence on the birth rate.

There are about 800 physicians, 200 of whom live in or round the capital San Juan. The country districts are poorly supplied. Many of the doctors of municipal and district hospitals receive 300 to 450 dollars a month, and some give good service in return, but according to the author many more give poor service. There are 65 type A rural health units and 21 type B or purely public health units. These serve the country districts but they are not described—the service at some is said to be very poor.

There are 8 district hospitals and 7 others or planned—most of these are good and have recently improved under the guidance of Dr J. A. Pons, the commissioner of health. There are municipal hospitals in several towns, some good, some not. Apparently the difficulty is largely due to the political domination of hospital operation and the employment of physicians who have poor ideals or no ideals at all. It would be wise to transfer these hospitals to the central government. Two hospitals for tuberculosis (and another projected) and for the insane and one leprosy colony are also functioning, and there are several large private hospitals and clinics, which do excellent work.

For medical education students go to the United States and few are now there. If this process can be continued, the demand for doctors will eventually be met. In addition there is the group of practitioners many of whom have been male nurses but who have expanded their activities and peak of themselves as minor surgeons. Their status was made legal in 1943 but many of their performances are regarded as injurious to the persons on whom they work. For post-graduate medical study the School of Tropical Medicine (which is conducted jointly by the government the University of Porto Rico and the Columbia University) is in the author's opinion the greatest single factor in improving educational standards in medicine. It offers training in public health and it operates a dispensary with 25,000 patients a year.

In the Virgin Islands the total population is about 30,000. Agricultural possibilities are slight and the economic future may depend on tourism. Government care has been the rule for many years in the provision of free



financial aspect of the project, the legal aspect of antimalarial operations and the maintenance of drained swamps. There are appendices reproducing the various forms used in the operation of the scheme, as also a summary of standing orders for maintenance workers and the provisions of a government ordinance relating to mosquito destruction. There are also a number of excellent photographs, maps and diagrams, among which a series of sketches by Mrs Gilroy deserves special mention.

The text is written with clarity and vigour, and contains a wealth of information relating to the essential requirements on which depend the success or failure of an antimalarial drainage scheme. Every sentence contains matter of practical importance to the field worker. The title suggests that the subject matter is limited to coastal swamp drainage, but the book will be of service to those engaged in antimalarial drainage in any type of terrain, for the basic principles on which the success of all such schemes depends are essentially similar. Moreover, though written primarily for health officers, it will be helpful also to others connected with antimalarial schemes, administrators and field workers alike. Health authorities in malarious countries will be well advised to order copies of this book for distribution to all members of their staff who are likely to be called upon to plan or supervise antimalaria drainage works. It might with advantage be circulated also to hydraulic engineers operating in such regions, who do not always appreciate the essential differences between swamp drainage as a purely engineering problem and as an *Anopheles* eradication measure.

G Coull

SANDOSHAM, A. A. *Malaria in Malai. A Handbook for Anti-Malaria Students*. With a Foreword by T SATO. pp xv+288, 22 figs & 8 pls (5 coloured). [Bibliography]. Reprinted with corrections 1945. Syonan [Singapore], Syonan Tokubetu-Si.

No claims to originality are made for the subject matter contained in this book. It is a compilation from many sources, put together in the form of lecture notes and then expanded into an elementary text book to suit the course of studies in malariology organized by the Health Department in Malaya.

The author divides his subject into seven sections. The first is mainly historical but also contains general remarks on blood parasites and stains, the second section [part of which will have to be rewritten since the discoveries of SHORTT and GARNHAM] introduces the beginner to the malaria parasites, questions of immunity, climate, endemicity and epidemicity in Malaya. The anopheline mosquitoes of the country are dealt with in the third section. The fourth section is devoted to a good practical description of malaria and anopheline survey methods and the making of survey maps and reports. Section five deals with control and describes the usual well-tried ways of draining, oiling and so on, followed by notes on treatment and drug prophylaxis. Again, parts of this section need to be brought up to date. For example, the formulae for Dover's cream and Bamber oil are given but dimethyl phthalate is not mentioned. The various formulations of DDT are omitted, and there is no reference to paludrine. A useful brief section on culicine mosquitoes comes next and the seventh section contains appendices on instructions in microscopy and the preparation of thin and thick blood films and staining. Aids to the identification of malaria parasites describe side by side the appearances of the different species in thin and thick film preparations, and aids to the identification of seventeen out of some forty species of Malayan anopheline species include illustrated descriptions of the main distinguishing characters.

There is a full index, but no attempt has been made to give a full list of references to works which have been consulted or from which data have been

zones in this region, the first of which is completely submerged by the diurnal neap tides, the second for a few days monthly by the spring tides and the third only twice each year by the high equinoctial springs. The second zone in which occur extensive groves of the white mangrove *Avicennia nitida* is characterized by large-scale breeding of *A. melas*, whilst the first and third are comparatively innocuous. Control of breeding by means of larvicides had proved ineffective and recourse was therefore had to swamp drainage on an extensive scale.

The scheme was initiated in 1942 for the control of malaria among service and particularly among R.A.F. personnel. It was continued after 1944 as a permanent undertaking, financed from Colonial Development and Welfare funds. In all, more than six square miles of swamps lying within the urban district of Lagos have been successfully drained.

By a fortunate chance the R.A.F. personnel detailed for the project at the commencement of operations included a Norfolk hedger and ditcher, a borough council navvy and a landscape gardener's mate—all men accustomed to digging and hard manual labour in general. To each of these was assigned a squad of 11 Africans for training and thus a nucleus of skilled diggers was created round which the main body of the labour force was subsequently built up. There can be no doubt that the success of the scheme was largely due to the high quality of the supervisory staff and to the sustained enthusiasm which Dr Gilson was able to maintain among all those engaged in the operations.

Since no satisfactory attempt at drain excavation can be made in a swamp subject to flooding until the tides are excluded, the first stage in swamp drainage is the construction of a protective bund. Contour drains are dug following the margin between the swamp and the higher land behind it, and these are connected to the main drains so as to conduct the water collecting in them by the shortest route as possible to the lagoon. Subsidiary drains are constructed where these are found essential but as in every good drainage scheme all drains are restricted to the absolute minimum necessary for the efficient drying of the land.

Sluices, constructed with the aid of coffer dams, are placed in the bund at the outfall of each main drain. These are operated by hand, the possibility of using automatic sluices having been ruled out because of the very small head of water in ched. Breeding of anopheline mosquitoes is very rare in well-maintained drains as also in the numerous shallow floodings in the bunds. Fortunately these latter have not proved a serious cause of damage to the banks.

The organization of swamp drainage in the Lagos area is based on the task system, which is preferred on the grounds that it entails a minimum of supervision, needs less attention to punctuality, allows of accurate estimation of quantities of work and is popular with labourers who know that the better they work the sooner they will be allowed to go home. Special attention is given to the training of foremen and the necessity for efficient backing in the execution of their duties on the part of the European staff is emphasized.

The financial aspect of the project is treated in detail, the method of costing, daily costs being of special interest. By the system adopted a balance is struck from day to day between available funds and amount expended. This situation, viewed in the light of weekly progress indicates whether or not the two are keeping pace. The cost of maintenance when the scheme is complete and continued eradication of anopheline breeding, averages about 15% of the original outlay. A programme decrease in annual expenditure is expected after the consolidation of the earth work is complete.

The book comprises two main sections: the first gives a detailed account of the practice of swamp drainage, the second describing in comprehensive terms the organization of a swamp drainage scheme. Other sections deal with the

financial aspect of the project, the legal aspect of antimalarial operations and the maintenance of drained swamps. There are appendices reproducing the various forms used in the operation of the scheme, as also a summary of standing orders for maintenance workers and the provisions of a government ordinance relating to mosquito destruction. There are also a number of excellent photographs, maps and diagrams, among which a series of sketches by Mrs Gilroy deserves special mention.

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There is a full index, but no attempt has been made to give a full list of references to works which have been consulted or from which data have been

extracted. Twenty publications are listed, none of which is later than 1940. The coloured plates illustrating malaria parasites seem to be reproductions of coloured pencil drawings.

[The book was first published in 1944 and reprinted in 1945. The author has undoubtedly performed a useful service in gathering together into one volume the kind of information necessary to and, indeed, often demanded by students of malaria and mosquito control. The absence of references to the more recent advances in knowledge made during the war years and since the volume first appeared, is unfortunate but understandable, and it is to be hoped that settled conditions will soon permit the new knowledge to be incorporated in the next reprinting.]

*H. S. Looser*

ADOLPH, E. F. and Associates [Dept. of Physiology, University of Rochester]. *Physiology of Man in the Desert*. pp. xiii+357 184 figs. 1947 New York & London Interscience Publishers, Inc. [30s.]

During the war years much research on the responses of man to his thermal environment was sponsored by the United States Office of Scientific Research and Development and prominent among the scientists engaged on this work were the authors of this book. Adolph's work on water balance is well known, and in their wartime studies he and his colleagues were largely concerned with the water and heat metabolism of man in the desert.

The book is a cooperative effort of the members of the Rochester Desert Unit. It deals with body heat exchanges, sweat formation and water turnover in a general way, and then turns to specific problems of life in the desert. Rates of sweating, urinary excretion, fluid intake water requirements and water shortage are discussed. Then come chapters dealing with various aspects of dehydration, on survival without drinking water in the desert, and on the water losses of men on life rafts. In a chapter comparing tropical with desert conditions there is a useful discussion of the physiological assessment of environmental stress. For comparing the stresses imposed by desert and tropical environments, the authors use as their index the rate at which the body gains heat from the environment.

The penultimate chapter by Adolph, includes a discussion of the factors which render and keep a man desert-adapted. There is a final chapter of summary and conclusions, and the last few pages of this give practical conclusions of great value to those responsible for men in the desert.

This book is a highly important contribution to environmental physiology. It contains a wealth of information sometimes in tabular form sometimes in clear diagrams, and sometimes in the form of beautifully produced maps.

Although it appears as one of a series of monographs on the physiological sciences it will appeal to many who are not physiologists. It is clearly written and extremely interesting and it is well produced.

*Thomas Bedford*

PASSMORE, R. [M.A., D.M. Oxford, Captain, Indian Medical Service Nutrition Research Laboratories, Indian Research Fund Association, Coonour S. India]. *Nutritional Diseases in India described for Students and Practitioners*. pp. ii+126+1 15 figs. on 13 pls & maps. 1949. Calcutta U.N. Dhur & Sons Ltd. [Rs. 10]

The book is written primarily for the medical student and practitioner in India. The author feels that hitherto these categories have fallen between two stools—the detailed book on nutrition written for the research worker and the popular book on nutrition written for the non-medical public.

The first chapter is appropriately on the causes of sickness and death in India and their relation to diet. The opening paragraph could not have been better chosen for it consists of Sir Alexander Russell's oft-quoted words on the overriding importance of the recognition of the dietary defects of the population of India whatever disease is being specifically considered from the preventive aspect. The author then proceeds to consider the causes of death in India and to point out the part played by defective nutrition in each case, he has usually backed his argument by statistics from the Public Health Commissioners' reports or from those of provincial directors of public health. The diseases discussed include malaria and "fever", dysentery and diarrhoea, respiratory diseases, and leprosy, infantile and maternal mortality are also included. Most of the arguments are well-known to the reviewer, but this will probably not be the case with the general reader who may not be quite so familiar with the subject and the author will certainly make his point. Somewhat surprisingly most of his statistical data are at least 10 years old.

The chapter ends on the note on which it began, the author points out that the nutrition problem can only be tackled by revolutionary changes in agriculture and in the social, political and religious life of the community, and that, although it is not the doctor's business to bring these about, it is his business to point out how necessary they are.

The second chapter is on malnutrition, and generally speaking it is a very satisfactory one. The author has described the stigmata of malnutrition without necessarily specifying which particular food deficiency is responsible for each defect. This is a healthy modern tendency in nutritional studies, it has been necessitated to some extent by the obviously mixed aetiology of most clinical manifestations of malnutrition, and by the many mistakes that have been made in the past through unjustifiable dogmatism. The chapter concludes with a discussion on treatment of malnutrition. Interpolated in the middle of this chapter, under a section headed "The Blood and Urine", are a few remarks in very small print on sprue and ariboflavinosis. The impression conveyed is that this was an afterthought, late in the production of the book when the author suddenly discovered that he had not mentioned these two words, neither of which as words he appears to like.

His paragraph on sprue opens and concludes thus —

"Sprue is a condition very similar to the picture of malnutrition already described. nutritional diarrhoea is a sound descriptive diagnosis, preferable in most instances to 'sprue', a Dutch word apparently meaning an inflammation of the tongue." It is felt that the after-thought, if it was one, was unfortunate and that it would have been better to have ignored the disease, which as it is seen in the European does not, in the reviewer's opinion, play any part in the nutrition problem of the native of India.

In Chapter 3 is given a good description of certain specific deficiency diseases, beriberi, pellagra, scurvy and rickets and osteomalacia.

The next chapter is on anaemia in relation to nutrition. It is not one of the better chapters of the book, the author does not seem very familiar with the subject and did not write a very orderly chapter, although he started appropriately with physiological considerations and a reference to Whipple's work on blood formation and diet. His short excursion into haematological methods was unfortunate, for no very good reason he chose to describe the method of calculation of the mean corpuscular values, MCV and MCHC, and got the first one wrong (possibly a misprint, but it is repeated).

The next two chapters are again sound ones, they are on "Diseases probably due to food poisons" and "Miscellaneous Diseases in which the Errors in Diet may be a Contributory Factor", respectively. However, the publishers evidently did not approve of the author's doubts and have called them

"Diseases due to Food Poisons" and "Diseases caused by Errors in Diet" on the page headings. The former include lathyrism and epidemic dropsy and the latter tropical ulcer, goitre, peptic ulcer, diabetes, dental disease, carbuncles of the liver and urinary stone. The author, however, is unequivocal in his opinion that diet has little to do with stone formation.

The book concludes with a number of useful appendices, food analyses, diet tables, etc.

It is a book that will serve its purpose well. It is pleasing to handle and read and the price is moderate. The illustrations are mostly good and relevant but it would have been better if they could have been distributed into their appropriate places in the book instead of being concentrated at the beginning. Finally, it is singularly free from misprints. However for the sentence "The normal stimulus of thirst appears to be in obedience" the reviewer who has also published books in India, extends his sympathy to the author in the words of John Bradford, "But for the Grace of God there goes

L. E. Vajpey

# TROPICAL DISEASES BULLETIN

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## RABIES

PIRINGER, W Die Impfmethode gegen Lyssa nach Semple - [Anti-Rabies  
Vaccination by Semple's Method] *Ztschr f Hyg u Infektionskr* 1944,  
Nov 12, v 126, Nos 1/2, 7-35, 1 fig [26 refs]

During the period 15 5 1938-31 12 1942, when Semple's phenolized vaccine was used in Vienna for the treatment of bitten persons, there occurred but one case of rabies (23 days after infection) and one non-fatal case of post-vaccinal paralysis among the 1 735 persons treated

Close scrutiny of the records of treated persons, classified according to the condition of the biting animal, permitted transfer of a very large number from category C (those bitten by animals simply suspect) to a new category E (those in contact with but not bitten by, an animal which, although unknown, was yet most probably healthy) Patients in category E and in category D (where the biting animal proved healthy after observation or laboratory inoculation tests), having been at slight, if at any, risk, are not taken into account when the author calculates the incidence of rabies among the treated, but are included when he estimates the frequency of paralytic accidents His evaluation of anti-rabies treatment, being based solely on the results obtained in respect of persons actually at risk shows no favourable bias, therefore, *vis-à-vis* the method employed

Apart, however, from the evidence based on statistics improperly considered, favourable results of anti-rabies treatment in recent decades may be traceable to a diminished virulence of the street virus present in some particular region such as Austria a diminution probably effected by the occurrence of rabies in only one species

In the author's view, until reports from Institutes, dealing with the successes and failures of anti-rabies vaccination, contain wholly accurate and comprehensive data on the occurrence of rabies among animals living in freedom or captivity and on the character of the street virus within the radius of each Institute's sphere of activity, a comparison between statistical series cannot be attempted and the value of the different methods of vaccination cannot be assessed

G Stuart

SIEGLER, A M Encephalitis due to Antirabies Vaccine Report of a Case  
*US Nat Med Bull* 1948, July-Aug, v 48, No 4, 620-25 [11 refs]

A case of an encephalitic reaction due to anti-rabies vaccine in a child with no history of allergy is described An 8-year-old Negro boy, bitten on the forearm by a stray dog, had had the wound cauterized immediately and on

following day had begun a 14-day course of anti-rabies treatment with phenolized (Semple) vaccine. Two days after completion of treatment, the child developed a staggering gait and complained of headache, drowsiness and double vision in the right eye. In the course of the next two days prior to his admission to hospital, the child experienced generalized weakness and was observed to drool to masticate only with great difficulty and to have fine tremors in all the extremities when sitting or standing. His tongue deviated to the right and his speech was slurred and unintelligible. Dr. Wassner and headache persisted. His temperature rose to 101.6°F. but there were no chills, vomiting or convulsions and there was no incontinence.

Clinical examination on the patient's first day in hospital revealed *nil* *ab* *norm* that in the fundus there was physiological cupping, but no choking or papilloedema. The tongue protruded towards the right and drooling was noted but associated pharyngeal and palatal movements were normal. No gross abnormal movements were observed. The abdominal and cremasteric reflexes were absent and the deep tendon reflexes all diminished, but the right triceps was more active than the left and the right biceps was more active than the left. Babinski's sign was definitely extensor on the right but equivocal on the left. Sensation was grossly intact and there were no cerebellar signs.

On the second hospital day a definite left central facial paralysis was noted and a paresis of the left upper eyelid.

By the seventh hospital day the extra-ocular muscles were normal, the facial paralysis had subsided and the patient had regained almost all of his muscle power. On the twelfth day the child was completely symptom-free and was discharged from hospital in excellent condition. In this case it is worthy of record that investigations at the Rockefeller Institute to exclude any known type of virus encephalitis were made on the cerebro-spinal fluid and blood and were reported as negative.

In his commentary on the frequency, aetiology and treatment of the paralytic accidents of anti-rabies treatment the author draws attention to the already sufficiently established facts (1) that children, who suffer so frequently from bites, are infinitely less liable to paralysis than adults (2) that the aetiological agent is undetermined and (3) that there is no specific treatment for the condition.

G. Stuart

## MALARIA

WEYER, F. Bemerkungen zur gegenwärtigen Malariafrage in Deutschland.  
(On the Present Malaria Situation in Germany. Reprinted from *Zeitschrift für Tropenkrankheiten* 1948 Jan 30 Nos. 34-36 9)

Malaria in the present-day Germany seems to be a really serious problem. The extension of the theatres of war to malarious countries, the introduction of prisoner of war and the return of their own soldiers to Germany have brought about a large increase of cases. Since 1941 there have been 387 cases in prisoners of war in Brandenburg Province, 73 in the troops, 53 in foreign workers and 11 in the civilian population. 9 of these have acquired the infection locally. In 194 there were 18 autochthonous cases, in 1943 8, in 1944 141 mostly in a small focus on the Tegeler See to the north west of Berlin. After the war ended conditions became much worse. Return of troops and prisoners, the stream of refugees lack of proper supervision, cessation of all reasonable measures of hygiene or prophylaxis, the lowered constitutional strength of the people all played part. There is an endemic focus (malaria) in East Prussia.



## Malaria

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The author compares the present condition with that after the first world war. In 1918-19 at Emden malaria station there were 6,839 cases and malaria was introduced during the war from the Balkan front. Small epidemics occurred in Emden in 1926 (571 cases), in 1938 (327 cases), in 1939 (213 cases) and thereafter fewer each year, 56, 16, 17, 10, 10, and 6 in 1945. Since then cases have been reported from Hamburg, Schleswig-Holstein, Lower Saxony, the Rhineland, North Württemberg, Karlsruhe, Mecklenburg and Pomerania in the Russian zone of Berlin, up to July 1946, 662 cases were recorded, of which 220 acquired the infection in Berlin itself, thereafter cases increased rapidly in this zone, at the beginning of September more than 1,000 had been registered. In the same year over 200 cases were treated in Frankfurt-am-Oder and its environs, 3 relapses and 197 fresh cases, in Schleswig-Holstein 470 cases, 190 autochthonous, STEINIGER, who reported this, estimates that the actual cases probably numbered twice this. In a transit camp at Friedland in 1945-46 Thonnard-Neumann stated that one in eight of 12,000 of those returning home suffered from malaria.

Various races of *A. maculipennis* are found in Germany, *A. m. maculipennis* in the hills, *A. m. atroparvus* on the coast and in brackish waters, *A. m. messeae* in the interior, the second of these is the vector in East Friesland, the third in Berlin. H. Harold Scott

BATISTA, Djalma. O paludismo na Amazônia (Contribuição à epidemiologia, à protozoologia e à clínica estudo sobre a febre biliosa-hemoglobinúrica; síntese) [Malaria in Amazonia] 212 pp, 10 charts [Bibliography] 1946 Rio de Janeiro Imprensa Nacional

This volume on malaria in Amazonia is based almost exclusively on observations made in Manaus, the capital of the State. It is claimed that the nosology of the town is more or less typical of that of the whole vast State. Manaus is situated on the River Negro some 18 km from its confluence with the Amazon. Its population is about 65,000. It has a general hospital, Santa Casa de Misericórdia. About one-fifth of all admissions to that hospital are on account of malaria. Malaria cases occur throughout the year, but the maximum incidence is in the months June to October, the peak generally occurring in August. These are the months of minimum rainfall, highest temperatures and lowest humidities when water levels are at their lowest. Discontinuous collections of stagnant water provide very favourable conditions for mosquito breeding at this season.

Over a period of 22 years malaria has been responsible for 21.4 per cent of the total deaths in Manaus, and tuberculosis for 13.5 per cent. These two chief causes of death are not unrelated, debility caused by malaria predisposes to infection with the tubercle bacillus.

*P. vivax* infections predominate. A description is given of clinical forms of malaria seen and of rare forms of the disease. Curative and preventive treatment are also considered.

Though malaria is the chief endemic disease of Amazonia, work for the amelioration of conditions should not be concentrated on malaria alone but rather directed to an all-round improvement of sanitary conditions. Special geographical considerations and the scarcity of the population in this vast area necessitate special measures. Norman Whit

SENEVET, G. Nouvelles espèces d'Anophèles [New Species of Anophelines] Arch. Inst. Pasteur d'Algérie 1948, June, v. 26, No 2, 149-61 [80 refs]

The author reviews the advances which have been made in the systematics of *Anopheles* in the ten years from 1938. In that period, eighty-seven new species (11-47)

have been described of which in the author's opinion about seventy-three have good claims to be recognized.

The paper gives a list of the new species and varieties with the type locality of each, grouping them under sub-genera. A very large proportion of these new species are described from the tropics of the New World, twenty-one of them from Brazil. The author is of opinion that some of these new names are frankly synonyms and that others are of doubtful validity. He then proceeds to discuss the limits and synonymy of certain difficult groups of sub-genera, e.g. the perplexing American *Myzomyia*. It is a matter of some interest that though many new species are described from the Old World sub-genus *Myzomyia* they fall easily into place in the existing scheme. This is not by any means true of some of the new American species. [It is suggested that the explanation is that owing to the careful scholarly work of EDWARDS, CHRISTOPHERS and others, our knowledge of *Myzomyia* is well founded. In contrast with this, a fog prevails over *Myzomyia* in the New World due in part to great natural difficulties but in part also to imperfect entomology. The position will grow worse if workers in tropical America are not prepared to exchange material, to take a wide international view and describe new species in comparison with what is already known.]

P. A. B. LON

REID, J. A. A Preliminary Note on Malayan Forms of *Anopheles barbatipes*. *Mal J Malaya*. 1947 Dec. v 2 No. 2, 1-3-7

The author produces evidence of the existence of at least two forms of *Anopheles barbatipes* in Malaya. For the present, one is called the dark winged form and the second the light-winged form. Examination of material in the collection of the Institute for Medical Research, Kuala Lumpur suggested that the dark-winged form was typically a mosquito of the coastal plains, while the light winged form occurred both inland in hilly districts and on the coastal plain. Recent collections confirmed this. Some evidence of a circumstantial nature also suggests that the dark winged form is a fairly formidable vector of malaria, while the light winged form is relatively unimportant in this respect. Work is now in progress to determine this point.

H. S. LEECH

EYLES, D. E., YOUNG, M. D. & BURGESS, R. W. Studies on Imported Malaria. 8. Infectivity to *Anopheles quadrimaculatus* of Asymptomatic *Plasmodium vivax* Parasitemia. *J. National Malaria Soc.* 1948, June v 7 No. 2, 123-33, 1 fig.

Persons infected with *P. vivax* often exhibit parasites in their blood in the absence of clinical symptoms of the disease. They are thought to be a particular danger to the community because of their liability unknowingly to infect mosquitoes. Over 2,000 *Anopheles quadrimaculatus* were allowed to bite 35 people in the asymptomatic stage of benign tertian malaria. The patients belonged to three categories, namely just prior to a relapse, in between attacks and at the end of attacks. All three groups infected the mosquitoes. 23 per cent. of the batches became infected and 1 per cent. of the total mosquitoes. Mosquitoes which had fed on patients with symptoms of malaria became more heavily infected (half the total batches) which was only to be expected as the degree of parasitaemia in this group was higher than in the others. The authors showed that the infection in the mosquito was correlated both with the total parasite count and the male gametocyte count.

P. C. C. GARNHAM

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YOUNG, M D & BURGESS, R W Studies on Imported Malarias 9 The Comparative Susceptibility of *Anopheles quadrimaculatus* and *Anopheles maculipennis freeborni* to Foreign *Vivax* Malaria J National Malaria Soc 1948, June, v 7, No 2, 134-7

The infectivity of *P vivax* to two important anophelines of North America (*A quadrimaculatus* and *A maculipennis freeborni*) was compared under identical conditions. The strains of *P vivax* came from the Pacific, Africa, West Indies and Burma. In all, 921 *A quadrimaculatus* gave a 44.2 per cent infection rate, 830 *A maculipennis* gave a 52.7 per cent rate. The latter species also showed more numerous oöcysts. The relative susceptibility of 5 American carriers of this form of malaria was calculated to be as follows: *A maculipennis* — 100, *punctipennis* — 86, *quadrimaculatus* — 84, *pseudopunctipennis* var *pseudopunctipennis* — 35, and *albimanus* — 2. [See also YOUNG et al, this Bulletin, 1947, v 44, 275] P C C Garnham

VARGAS, L & MATHESON, R Estado actual del *Anopheles earlei* Vargas 1943 y *Anopheles occidentalis* Dyar & Knab 1906 con claves para larvas pupas y adultos del llamado complejo *maculipennis* de Norteamérica [Position of *Anopheles earlei* and *Anopheles occidentalis* with Keys to the Larvae, Pupae and Adults of the *maculipennis* Group of North America] Rev Inst Salubridad y Enfermedades Trop Mexico 1948, Mar, v 9, No 1, 27-33, 6 figs on 2 pls [12 refs]

REY, H Revista de nuestros conocimientos sobre vectores de malaria en Colombia [Review of Known Malaria Vectors in Colombia] Tijeretazos sobre Malaria Venezuela 1947, Mar. & June, v 11, Nos 1/2, 30-32

The author reviews the position of the known vectors of malaria in Colombia proved by various investigators up to December 1946. A table shows the results of stomach and gland dissections of the species, together with the place and date of origin and the name of the workers reporting them. The following species have been found to be naturally infected with plasmodia: *A darlingi*, *A punctimacula*, *A albistarsis*, *A pseudopunctipennis*, *A neivai*. H J O'D Burke-Gaffney

PINOTTI, M, RACHOU, R G & FERREIRA, M O Algunos aspectos epidemiológicos de la malaria en el Litoral Sur del Brasil en la zona de transmisión por anofelinos del subgenero *Kerteszia* [Certain Aspects of the Epidemiology of Malaria in the South of the Coast of Brazil, in an Area of Transmission by *Kerteszia*] Tijeretazos sobre Malaria Venezuela 1947, Mar & June, v 11, Nos 1/2, 1-25, 10 text figs (3 maps) & 4 figs on 2 pls [26 refs]

[It will be remembered that in certain parts of Tropical America, where rainfall is high, large numbers of Bromeliad plants grow on limbs and trunks of trees. They hold water among their leaf bases, and *Anopheles* of the specialized subgenus *Kerteszia* breed in them.]

In the extreme south of Brazil, in parts of the States of Parana, Santa Catalina and Rio Grande del Sul, one finds abundant Bromeliads and three species of *Kerteszia*, *bellator*, *cruxii* and *homunculus*. The paper discusses their biology and methods which have been used for destroying Bromeliads and to control mosquitoes. The area is malarious, but it cannot be accepted that the infections are to be attributed solely to the *Kerteszia*. P A Buxton

- i. MARGRAITH, B. Pathological Processes in Malaria. *Trans. Roy. Soc. Trop. Med. & Hyg.* 1948 May v 41 No. 6 657-69
- ii. ANDREWS, W. H. II. The Liver Lesions in Malaria. *Ibid.* 1949-VI, 3 figs. on 2 pls. 69 refs. relating to the above two papers in a combined list at pp. 702-4 and Discussion at pp. 706-13 1 pl., 13 refs.]

i From a study of the literature it would appear that the tissue changes occurring in malaria infections are of two types—(1) continuously progressive and (2) periodic. Anoxaemia, vascular and circulatory disturbances are associated with the first of these—the malaria paroxysms with the second.

Anoxaemia results from defects in pulmonary ventilation and blood circulation, and from red cell destruction with consequent deficiency in oxygen-carrying capacity of the blood—parasitic invasion of the red cells and intra-vascular red cell agglutination with the formation of "sludges" (HAXHALL *et al.* see this Bulletin 1943 v 40 584), a result of the generalized anoxia, add to this.

During the cold stage of a malaria paroxysm there is peripheral vascular constriction, a rise in blood pressure, and slowing of the circulation time. During the hot stage there is peripheral dilatation and a fall in blood pressure with increased cardiac output. The heart rarely fails, but a condition of medical shock may result from generalized vascular collapse with loss of circulating blood volume, indicated by an increased cell count and haemoglobin concentration.

Local circulatory changes are influenced by the vascular anatomy of the organs concerned, or by reflex reactions. Reflex vascular mechanisms are known to exist in the kidney and in the liver lobules. Mechanical obstruction to circulation occurs in some tissues as a result of swelling of the vascular endothelium, with an accumulation of leucocytes, parasitized red cells and debris. True thrombosis may occasionally occur. A local loss of fluid from circulating blood, with impaction of the red cells is a major factor in the production of vascular stasis. This takes place particularly in organs with capillaries normally impermeable to protein—as the brain and the heart—and the result is a local tissue anoxia.

The generalized circulatory changes during a malaria paroxysm are probably of central origin and may be due to stimulation, and possibly concomitant inhibition, of certain vasomotor centres, especially in the hypothalamus attributable to the release of a diffusible substance during parasitic proliferation. Loss of body fluid by sweating and diarrhoea is a minor contributory factor. Changes in the vascular endothelium are evident histologically and by induction on physiological grounds. Tissue anoxia is probably a factor in their production. Evidence is forthcoming that any malarial toxin plays a part in their causation. The consequent increase in permeability of the affected vessels allows protein and fluid to escape into the tissues.

In the brain, anoxia due to progressive capillary stasis leads to degenerative changes and necrosis of surrounding tissue. The cerebral lesions of malaria are not peculiar to the disease but occur in other conditions, as severe anaemia, hyperthermia, mechanical obstruction of the large vessels to the brain, and narcotic poisoning. The stasis or near stasis seen in the cerebral capillaries is temporary and reversible—it is not associated with true agglutination or clumping of the involved red cells. On resolution of the stasis the escape of protein through the vessel wall stops and with the return of fluid circulation through the vessel recommences.

While vascular stasis is common in the brain it is uncommon in the liver and it may or may not occur in other tissues. Variations in the permeability to protein of the endothelial cells of the vessels in the various organs may afford



to unpublished data which show that *P. falciparum* persist apparently unaltered for at least 18 hours but that they have vanished by 36 hours after death.

Dr MARGATROYD suggested that if changes in the permeability of the cerebral vessels in malaria permit the escape of protein through them an increase in the protein content or volume of the cerebrospinal fluid would be expected. This does not consistently occur. Dr NICOL stated he had occasionally seen cases of peripheral circulatory failure in cases of *P. vivax* infection the condition persisted for several days after specific antimalarial treatment. Lt.-Col. MAXTOLD reported a case of *P. vivax* infection with extraordinary hyperpyrexia and a dry theca, which at post mortem showed blocking of the choroidal plexus by parasitized cells.

MARGATROYD in reply referred to the lesions occurring in the suprarenals and the pituitary and their relation to the pathology of malaria. He reformed that on a study of the literature there was little evidence for including cardiac failure as a common complication of malaria. It is vascular collapse rather than cardiac failure which is the commoner cause of death the two are often confused.

A. R. D. ADAMS

JASSIAS, C. A propos des fausses réactions de la syphilis dans le paludisme [False Positive "Syphilis Reactions" in Malaria.] *Bull. et Mém. Soc. Méd. Hôp. de Paris*, 1948, No. 24/25 824-8.

The author discusses briefly the false positive serological reactions encountered with the use of different tests for syphilis in persons suffering from malaria. In 25 years experience he has examined tens of thousands of sera from malaria patients, and has never found the Hecht reaction positive (save in leprosy) provided that the technique is accurate and the reagents carefully controlled. He finds an antigen made from human heart the best. Occasionally the Hecht reaction was positive but transient during the eruptive stage of measles.

H. J. O'D. BURKE-GAFFNEY

BROOKS, M. M. & DONALDSON, A. W. Transfer of Malarial Parasites between Blood Films during Mass Staining Procedures. *Pub. Health Rep. Wash.*, 1948, July 30 v. 63 No. 31 991 1004 2 figs.

This paper must have given many field malarialogists "much to think." The authors appear to have demonstrated the danger of false "positives" when slides are stained in bulk for the detection of malarial parasites.

Were the methods employed in these experiments widely used in malaria surveys, they would appear to invalidate many of the published reports. In order personally to check the results the reviewer stained batches of slides put up by the method described and was satisfied that transfers of blood did actually take place from slide to slide in a varying proportion of cases.

On the other hand, such transfers were not detectable when mixed infected and non-infected or mammalian and a man blood slides were stained together in the upright position in ordinary staining dishes where the distance between neighbouring slides is considerably greater than when the slides are tightly separated by pieces of cardboard at one end as in the technique used in the experiments under review.

In the latter case the separation is so small that actual contact between neighbouring slides is easily brought about by the handling necessary in the staining, manipulations or even in putting up the packs of slides. One may say therefore that the danger of transfer of blood from one slide to another has been proved by the authors under the conditions of their experiments but that this

does not invalidate previous survey results obtained by other methods of bulk staining [For the experimental methods employed, the reader is referred to the detailed description in the text] H E Shortt

IPF, H F Zur klinischen Brauchbarkeit der Melaninserumreaktion von Henry bei der Malaria (Modifikation nach Trenz) [The Clinical Value of Trenz's Modification of Henry's Melanin Reaction] *Klin Woch* 1948, May 1, v 26, Nos 17/18, 274-6, 3 figs [12 refs]

If direct examination of the blood by the thick drop method fails to reveal malaria parasites, there is need for some diagnostic means for existent or latent malaria. Twenty-one years ago Henry brought out his iron albuminate serum reaction, later the melanin reaction for serological diagnosis, but the fact that a similar reaction was given in several other diseases, such as tuberculosis, carcinoma, syphilis, leprosy, typhoid fever, pernicious anaemia and kala azar robbed it of most of its value. The author discusses this and Trenz's photometric modification of the original test and shows that readings of over 56 are alone of practical use and that below this the test is not reliable. Comparing the melanin-serum reaction (macroscopic and photometric readings) with the water flocculation reaction, he found a parallelism between them, the sera remaining clear or showing mere turbidity are to be regarded as negative, those giving precipitation as positive, i.e., with photometric value of 56 or over. In latent malaria one may find lower levels, in such it is not so much the height of the reaction as its movement [variations], therefore a series of tests should be taken and the results plotted, if we are to obtain results of diagnostic and prognostic value. For the rapid diagnosis of malaria, consequently, the melanin-serum reaction is not to be relied upon. H Harold Scott

COURVÈS, J M Paludisme viscéral évolutif à symptomatologie cérébro-méningée [Malaria with Visceral Development of the Parasites and Cerebral and Meningeal Symptoms] *Bull Soc Path Exot* 1948, v 41, Nos 5/6, 368-71

BARASCIUTTI, A & DE NEGRI, U Nefropatie in malarici [Renal Disease in Malaria] *Acta Med Italica* 1948, May, v 3, No 5, 117-22 English summary

This paper contains a description of twelve cases of malaria in which concomitant renal disease was the outstanding characteristic. Nine presented signs and symptoms of acute glomerulo-nephritis, one of lipoidal nephrosis and two of chronic nephritis with uraemic syndrome. Eleven of the patients were infected with *P. vivax*, one with *P. falciparum*. The literature concerning the association of renal disease with malaria is considered at some length and the authors conclude that malaria may cause nephritis particularly in patients predisposed to renal disease. Many of the authors' patients come from the delta of the Po where they live in damp, insanitary dwellings, and are ill-nourished and underfed. Specific malaria therapy promptly produced a marked improvement, or disappearance, of renal symptoms. Norman White

DELANOE G Sur un cas de purpura hémorragique de nature paludéenne [A Case of Haemorrhagic Purpura due to Malaria] *Bull Soc Path Exot* 1948, v 41, Nos 5/6, 364-8

PERVIZ, M. Réactivation et traitement des formes chroniques de l'amébiase et du paludisme. [Reactivation and Treatment of Chronic Amebiasis and Malaria.] *Rev. Paludisme et Méd. Trop.* 1948, July, Aug. Sept. v. 4 Nos. 50, 51 & 52, 197-205.

A chronic concealed reticulo-endothelial type of infection with *P. falciparum* is described and the means of its revelation and treatment are discussed. Intravenous emetine and strychnine injections are advocated in the therapy of amebiasis.

A. R. D. Adams

MONK, J. F. Modern Therapy of Benign Tertian Malaria. *Brit. Med. J.* 1948 June 23 1221 5-1 chart. [16 refs.]

This review of recent developments in the treatment of *P. vivax* malaria is summarized by the author as follows:

"The ideal drug for the prevention and radical cure of benign tertian malaria has yet to be discovered.

"The dose of unaltered quinine therapy is recommended.

Suppressive and curative treatment with mepacrine is likely to be superseded by more recently discovered antimalarial drugs.

"Paludrine and chloroquine are probably equally effective in producing complete suppression of overt attacks of malaria in once-weekly dosage. Neither is able to prevent the establishment of *P. vivax* in the human host even by daily dosage, but paludrine has some inhibitive effect on the pre-erythrocytic form. Neither drug given alone is as successful as other forms of therapy in producing a low relapse rate.

"Pamaquin is a drug which deserves greater recognition as a safe medium for the elimination of *P. vivax* infections. Given as an adjunct in any course of antimalarial therapy it is of the greatest value in reducing the relapse rate. The toxicity of pamaquin is shown to be less formidable than is generally accepted.

No treatment so far administered to a large series of cases of naturally occurring B.T. malaria is more successful than quinine given concurrently with pamaquin. Paludrine given concurrently with pamaquin is equally successful.

Pentaquin given concurrently with quinine is likely to prove more successful in producing a lower relapse rate than any other therapeutic regime. The toxicity of pentaquin is approximately three quarters that of pamaquin.

"A 31-days intermittent course of quinine and pamaquin proved successful in the complete eradication of *P. vivax* infections in all patients followed up in a series of 45 cases. It is suggested that such a course is worth extended trials among chronic relapsing cases in a non-malarious area.

PARMER, L. G. Blood and Bone Marrow Concentration of Atabrine and its Role in Aplastic Anemia. *J. Lab. & Clin. Med.* 1948 July v. 33 No. 7 827-32.

Rabbits were given an intramuscular injection of 8 mgm. per kgm. of mepacrine (atabrine) dihydrochloride. They were killed at intervals and the distribution of mepacrine was examined; the results are shown in Table 1.

There was still a considerable amount of mepacrine in the bone marrow on the 4th day, by which time the plasma, erythrocytes and leucocytes of the peripheral blood contained hardly any. In chickens treated in the same way the distribution at 4 hours was similar to that in rabbits; by the fourth day all the tissues were free from mepacrine except the liver and spleen, which contained



TABLE 1

*Atabrine concentration (Mgm/kgm) in tissues of rabbits after an intramuscular injection of 8 mgm/kgm of atabrine dihydrochloride*

	Time after injection			
	4 hours	4 days	7 days	11 days
Rib marrow	5 08	0 89	0 37	Trace
Proximal femoral marrow	4 38	1 02	0 33	Trace
Distal femoral marrow	3 11	0 69	0 21	Trace
Plasma	0 08	Trace	0	0
Erythrocytes	0 27	Trace	0	0
Leucocytes	1 87	Trace	0	0
Lymph node	3 70	1 35	1 05	0 41
Thymus	2 70	0 57	0 10	0
Liver	7 78	1 25	0 46	0 05
Spleen	40 62	1 96	0 44	0 11

small amounts. Although the erythrocytes of fowls are nucleated, the concentration of mepacrine in them was less than a third of that in the leucocytes, apparently the high concentration of mepacrine in leucocytes does not depend principally on the presence of a nucleus.

Further experiments were made on five patients with the results shown in Table 3.

TABLE 3

*Blood and bone marrow concentration after oral administration of atabrine dihydrochloride to five patients \**

Patient	Condition	Leucocytes per cmm	Atabrine level ( $\mu\text{gm} \times \text{liter}$ )			
			Plasma	Erythrocytes	Leucocytes	Bone marrow
1	Malaria	7,000	42	—	—	836
2	Normal	5,500	77	55	—	1,200
3	Chronic myelocytic leukaemia	75 000	154	200	1,285	2,381
4	Chronic myelocytic leukaemia	75 000	250	392	1,589	—
5	Chronic lymphocytic leukaemia	90 000	53	57	1,864	—

\* Doses varied so that absolute levels between patients are not comparable.

Although the marrow specimens were greatly diluted by peripheral blood, the concentration of mepacrine in them was high. In a discussion of these findings, it is concluded that the alleged relationship between mepacrine and aplastic anaemia is not a direct one, rather it seems to depend on idiosyncrasy.

F. Hawking

SINGH, I. Mepacrine Dermatitis. *Brit J Dermat & Syph* 1948, Mar, v 60, No 3, 90-105, 4 figs [13 refs]

<sup>1</sup>Eighty-three cases of atypical lichen planus associated with suppressive mepacrine are described. The patients were all males, the majority were

aged between 21 and 35 and were employed as labourers on the Burma front mostly in a civilian capacity. Sixty-three had taken an average daily dose of 0.1 gm. mepacrine for 3 to 24 months; the remaining 20 had taken a larger dose for a shorter period.

In 73 per cent. of the cases the onset of the dermatitis was acute with a generalized erythema followed in 24 to 48 hours by crops of red itching papules. Later manifestations were follicular hyperkeratosis, papules, plaques and verrucous nodules.

Less commonly the onset was insidious, with glossitis, pigmentation of the mouth and tongue, a pigmented macular rash, pruritus, desquamation, or follicular hyperkeratosis. In four cases the eyes were involved, pigmentation of the conjunctiva and conjunctivitis being observed, and in one case corneal ulceration resulting in blindness. Scalp lesions were uncommon, and no case of permanent baldness was seen. The nails were not infrequently affected.

The biological picture showed acanthosis, an increase in the stratum granulosum, hyperkeratosis, parakeratosis, and sometimes spongiosis. There was increased vascularity in the papillae and the sub-papillary layer with considerable perivascular cellular infiltration. A pigment distinct from melanin and resembling mepacrine was seen both as free granules and within the phagocytes, especially in the papillary areas and around sweat glands.

In an attempt to establish the aetiology of this condition, the author observes that no case of similar dermatitis was seen in any person who was not taking suppressive mepacrine. He was able moreover to produce exacerbation of the condition by giving mepacrine to the affected patients, and to reproduce it in normal subjects by giving the drug in a dose of 0.4 gm. daily for 17-32 days.

The severity of the disease appeared to be related to the amount of mepacrine stored in the skin. The result of a prolonged course of mepacrine was to produce a slow rise in the skin mepacrine level, which fell more slowly than the plasma mepacrine after the drug had been discontinued. In general the disease was most severe in patients with low body weight; the severest cases being met with in patients weighing between 84 and 102 lb. Dosage should therefore be determined by body weight rather than age.

Treatment was designed to secure rapid elimination of the drug by giving fluids and by increasing the acidity of the urine. The nutrition was improved with a high protein diet and added vitamins. Generally it was advisable to remove patients to a cooler climate. [See also this Bulletin 1947 v 44 499-503.]

H. T. H. Wilson

EL DIN NOUR EL DIN G. Toxic Psychosis as an After Effect of Atabrin.  
*J. Roy. Egyptian Med. Ass.* 1948, June v 31 No. 6, 489-500 [15 refs.]

The author in 1933 saw a medical student who developed mania with delirium and hallucinations after intravenous atabrin (mepacrine). He recovered within a few days. In 1944-45 atabrin was used on a large scale for malaria treatment at the research institute, Cairo: three patients showed mental symptoms (two of these three had the drug parenterally). The drug is now used as a tannicide: a single dose of eight tablets is given, followed an hour later by a purge. No mental symptoms have resulted from this treatment. Very recently atabrin has been tried as an amoebicide: 3.51-4.5 gm. being given in 5 days. No mental symptoms have resulted in the 35 cases so treated.

Some details are given of the three patients who developed toxic psychoses while under antimalarial therapy, and the literature on the subject is touched on. [See also this Bulletin 1948, v 45 650.]

I. R. D. Lines

## Malaria

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LUCENA, D T Tratamento da malária pelo aralen [Treatment of Malaria by Aralen] *Rev Brasileira Med* Rio de Janeiro 1948, Apr, v 5, No 4, 269-79, 4 graphs English summary

Aralen is chloroquine diphosphate This paper is already so condensed that abstraction is hardly possible The total number of patients treated was small, 83, of whom 40 were adults and 43 were children Infections were by all three malaria parasites and the criterion of cure was disappearance of clinical symptoms and failure to find the parasites in thick smears on three consecutive occasions Adults were given total doses of 1.5-2 gm (occasionally 2.5 gm) in divided amounts spread over 1-3 days The 43 children were divided into four age-groups 0-4 years, 4-8, 8-12 and over 12 years and for these nine different regimens of treatment were tried The results can, therefore, only be summarized briefly (1) *P vivax* infections, clinical symptoms cleared up in 24 hours and parasites in the same time in four-fifths, and in two days in the rest [would not this occur naturally in *P vivax* infection?] (2) *P falciparum*, clinical symptoms again cleared up in 24 hours and trophozoites disappeared from the blood, gametocytes persisted for several days (3) *P malariae*, clinical symptoms cleared, as with the other parasites, in 24 hours, but the plasmodia were found for a little longer than in the case of *P vivax* but not so long as *P falciparum* In the above dosage there was no sign of any toxic action of the drug

H Harold Scott

ENRIQUEZ-NAVARRO, A F & ROGNONI M Uso del Aralén (Cloroquina Winthrop) en el tratamiento de la malaria aguda en niños [Aralen (Chloroquine) in the Treatment of Acute Malaria in Children] *Archivos Hospital Santo Tomas* 1948, Jan.-Mar, v 3 No 1, 35-8

REITSEMA, R H The Chemistry of 4-Hydroxyquinolines *Chemical Reviews* 1948, Aug, v 43 No 1, 43-68 [190 refs]

SIMMS, B R & KIKER, C C Temporary Dewatering in applying Deepening and Filling to permanently eliminate Mosquito Breeding Areas in Tennessee Valley Authority Impounded Reservoirs *J National Malaria Soc* 1948, June, v 7, No 2, 100-108, 6 figs

The problem of malaria transmitted by *A quadrimaculatus*, which breeds in waters along the margins of reservoirs in the Tennessee Valley, is dealt with by permanent elimination of the breeding areas, this involves two methods —

(a) Deepening and filling, (b) Diking and dewatering

These methods have been described by BISHOP and GARTRELL, this *Bulletin*, 1945, v 42, 184

Dewatering involves the installation of a permanent pumping station with attendant recurrent annual costs, moreover, for control of mosquito breeding, this method is not as satisfactory as deepening and filling This paper describes the initial use of temporary diking and dewatering to facilitate deepening and filling procedure under favourable engineering circumstances, the cost of the temporary measures in this instance were 5-10 per cent of the total deepening and filling project It is believed that this temporary dewatering method, by means of specially designed pumps, will be widely used to extend deepening and filling projects

R Ford Tredre

By exposure of caged mosquitoes to similar sprayed surfaces it was determined that 4 and 5 per cent concentrations will produce rapid kills of *Anopheles quadrimaculatus* 69 and 68 days after application of the insecticide. The lesser concentrations were not so satisfactory.

Application of residual insecticides in one anopheline shelter reduced the numbers of *Anopheles quadrimaculatus* in adjacent similar shelters. These field experiments were conducted during 1946 in the vicinity of a reservoir in South Carolina, U.S.A.

R. Ford Trice

ELMENDORF, J. E., Jr. assisted in Field and Laboratory Operations by H. G. BARNHILL, M. T. HOCKENGA & M. TAKA. Second and Supplementary Report on Field Experiments to demonstrate Effectiveness of various Methods of Malaria Control. *Amer J Trop Med* 1948, May v 28 No. 3 45-53.

This paper should be read together with a previous one [this Bulletin 1947 v 44 882] recording survey results and techniques used. Five villages in tropical America in which malaria was endemic and carried by *Anopheles albimanus* were subjected to an initial survey over a period of nine months and then used for a comparison of the values of different control methods. Treatments were started in December 1945 except that in the first village treatment with oxychloroquine (no further description given) was started in April 1946. The effect on the spleen and parasite rates is summarized in the following table in which S.R. means spleen rate and P.R. parasite rate.

Control method used		Survey result								
		1945			1946					
		Apr	Aug	Dec	Apr	May	July	Aug.	Dec	
Oxychloroquine prophylaxis	S.R.	66.3	83.6	92.6	83.3			66.7	61.9	
	P.R.	41.8	8	82.3	41.0		12.5	26.7	8.9	
DDT residual spray	S.R.	62.5	63.7	91	74.2			81.3	62.5	
	P.R.	44.2	45.6	97.1	56.5			24.4	15.6	
Aircraft antilarval DDT	S.R.	61.6	87.7	90.7	86.6			66.1	64.8	
	P.R.	31.1	54.7	83.4	61.4			51.7	12.7	
Chloroquine prophylaxis	S.R.	60.7	67.7	97.9	8.9			69.0	56.8	
	P.R.	33.1	33.3	47.6	6.0	5.4		9.5	2.1	
No treatment	S.R.				94.8			94.5		
	P.R.				59.6			16.6	57.6	

The cooperation received in the village where oxychloroquine was used as a prophylactic was much less than in that where chloroquine was used, and comparison is not possible. In assessing results comparisons should be made between findings in the equivalent months in the treated and untreated periods. Notable features are the marked lag before the drop in the spleen and parasite rates in the villages where DDT was used as either a larvicide or an adulticide and the eventual production of highly satisfactory results. One single treatment with DDT as a residual spray produced this result whereas many prophylactic applications were made of DDT as a larvicide from aircraft (though it is not shown that this was necessary). The authors conclude that a very satisfactory result can be obtained by one annual treatment with DDT residual spray in which a 5 per cent solution of DDT in kerosene is applied at the rate

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of 300-400 mgm /sq ft (10 6-14 oz /1,000 sq ft), "associated with a certain amount of suppressive chloroquine administration" [From the data given this adjuvant would not appear to be needed] G Macdonald

WHITMAN, L The Prolonged Viability of Sporozoites of *Plasmodium gallinaceum* in Extracts of Washed Chicken Erythrocytes J Immunology 1948, July, v 59 No 3, 285-94

Experimental malaria has been handicapped by the absence of a suitable medium in which to retain sporozoites for injection into clean animals. Even in the fluid (heparinized plasma) recommended by TONKIN [this Bulletin, 1948, v 45, 243] the survival rate was not extended much beyond 24 hours. Whitman, however, has discovered a better medium which will prove of great value to workers in this field. It is an extract of chicken erythrocytes prepared in the following way. Heparinized chicken blood is centrifuged for 20 minutes at 2,500 r p m, the plasma is withdrawn and the cells are resuspended in volume of saline, and recentrifuged. The washing is done twice more and then the cells are centrifuged with a minimum of saline at 3,500 r p m for 30 minutes in order that their exact volume might be found. The cells are resuspended in four times this volume of saline and transferred to an Erlenmeyer flask of such size that the suspension lies one inch deep. It is then frozen in a dry ice chest, thawed at 37°C (warm water) and refrozen for another hour. It is thawed again and centrifuged at 3,500 r p m for 30 minutes to remove the debris. For use, this extract is diluted 1 in 10 with physiological saline and the diluent is used both as a fluid in which to dissect the mosquito's glands and for storing the sporozoites.

It was shown that few *P. gallinaceum* sporozoites died in this fluid during the first 24 hours and many lived up to 72 hours, even at 25°C. The addition of penicillin (500 units per cc) is said to have no adverse effect on the sporozoites [but the experiments were not done on a quantitative basis, and it is possible that only a proportion survived this treatment]. An interesting observation was made on the inhibitory effect on sporozoites of extracts containing mosquito thoracic tissue. Two birds out of six failed to become infected and in the remaining four, the incubation period was prolonged. [It is desirable that this work should be confirmed on a larger scale, because if it is so confirmed, it would require that sporozoites used for infection purposes should be obtained from dissected glands only and not from ground-up thoraces, which is a common method at present.] P C C Garnham

DESCHIEENS R & PICK F Sur la non-inoculabilité de l'embryon de la poule domestique par le sang infecté par *Plasmodium gallinaceum* Brumpt 1935 [Failure of Blood Infected with *P. gallinaceum* to Infect Chick Embryos] Bull. Soc Path Exot 1948, v 41 Nos 5/6, 353-6

JOHNSON, H A & AKINS, H The Effect of One Plant Extract and of certain Drugs on the Development of *Plasmodium gallinaceum* in *Aedes aegypti* J National Malaria Soc 1948, June, v 7, No 2, 144-7

Various substances were tested on *Aedes aegypti* to observe their effect on *P. gallinaceum* infections. The tests were performed by allowing the mosquitoes, throughout the period immediately after emergence to 14-20 days after the infective blood meal, to feed on cotton sponges moistened with 2 per

cent. sugar solution plus the test drugs. The following had slight or no effect on the development of sporozoites —

Atabrin dihydrochloride—0.15 gm. 1.3 gm. per litre.

Plasmoquine naphthoate—11.2-67 mgm. per litre.

Chloroquine base—0.5-2 gm. per litre.

Red clover extract—filtrate from 11 blossoms in 100 cc.

The following substances exerted a very marked inhibitory action —

Quinine sulphate—0.67 gm. 1.33 gm. per litre.

Paludrine hydrochloride—0.18 gm.-0.435 gm. per litre.

In one experiment paludrine was withheld until the sporozoites appeared in the gland and the drug was then given for 5 days: no lethal effect on the sporozoites was observed after this delayed administration. Most of the drugs had some toxic effect on the mosquitoes and the results suggested that if higher doses could have been tolerated an inhibitory action on the sporozoites would have resulted. Chloroquine base was very toxic to the mosquitoes and showed little effect on development of sporozoites. P. C. C. Garnham

BISHOP Ann & BIRKETT Betty. Drug-Resistance in *Plasmodium gallinaceum* and the Persistence of Paludrine-Resistance after Mosquito Transmission. *Parasitology* 1948, July 39 No. 1/2, 1-5-37 [32 refs.]

A preliminary account of these experiments on the production of drug resistance in *P. gallinaceum* has been given by the authors (this Bulletin 1947 v. 44 909). For this purpose they maintained a patent infection in young chickens by giving intravenous inoculations of heavily infected hyperinfected blood at intervals of 24 to 48 hours in order to avoid the influence of exo-erythrocytic forms. The drug was given orally in aqueous solution on the day before inoculation and at least once per day thereafter proportional to the weight of the bird. Dosage was such that multiplication of erythrocytic forms was not interfered with. Tests were made at intervals on the normal and treated strain of *P. gallinaceum* to find if resistance had developed. In the case of atabrin (mepacrine) natural resistance to the drug was not increased after 6 months continuous treatment. With plasmoquine (pamaquin) a slight but definite resistance was detected after 8 months treatment. In the case of paludrine on the other hand, a forty fold increase of resistance was observed and was not lost after five serial passages through the mosquito vector. By the use of inocula, consisting mostly of exo-erythrocytic forms, from the pulsed spleen of a paludrine-resistant bird, it was shown that the exo-erythrocytic forms which arise from a resistant strain are themselves resistant to the drug, as are also the erythrocytic forms derived from them. Resistance to paludrine involved also resistance to a methyl derivative of the drug (M.4.3.3) but not to mepacrine or pamaquin. The immunological relationships of the normal strain were unaltered after it had been made resistant to paludrine.

J. D. Fallon

THOMPSON P. E., MCGINTY D. A., BISH D. L. & WILSON Mary L. Radioisotopes in Ducks and Canaries and its Effects on their Initial Malarial Infections. *J. Inf. & Dis.* 1948, July Aug. 83 No. 1 23-32, 2 figs. 1 r. (6.)

Radioactive colloidal iron mixtures containing  $Fe^{59}$  and  $Fe^{55}$  with half-life periods of 44 days and 4 years respectively were administered parenterally to ducks infected with *P. falciparum* and canaries infected with *P. malariae* in doses near the maximum tolerated to determine whether the radiation emitted ( $\beta$  and  $\gamma$  rays) had any effect on the multiplication of parasites. Radioactivity

of blood and tissues was measured by means of a Geiger-Mueller tube after digestion with acids followed by electro-plating of the iron on tinplate. In order to promote utilization of the injected radio-iron, the birds were rendered iron-deficient. Infection was produced by intravenous inoculation of blood. It was found that the iron injected intravenously or intraperitoneally was readily taken up by blood cells, but was more slowly converted to haemoglobin when given by the latter method. Before determination of the amount of radioactive iron in tissues of treated birds, blood was repeatedly withdrawn and replaced by normal citrated blood and saline and in addition the tissues were washed in water. Liver, spleen and bone-marrow contained the greatest amounts of the active material. Radio-iron was also detected in the excreta of canaries after intravenous administration of the substance.

Histological examination failed to reveal damage to organs or leucocytes due to radiation. There was no significant difference in the survival rates of birds receiving natural iron or radio-iron and any toxic effects appeared to be due to the metal itself rather than to radiation emitted. Radio-iron did not affect the course of *P. cathemerium* infections in canaries or of *P. lophurae* infections in ducks, as judged by parasitaemia and morphology of the parasites, in spite of the fact that the accumulation of pigment in the schizonts permits the maximum exposure to radiation during division.

J D Fulton

PIEKARSKI, G. Experimentelle Untersuchungen zur Frage der Atebrinfestigkeit der Malaria-Parasiten [Experimental Investigations concerning Mepacrine (Atebrin)-Resistance of Malaria Parasites] *Ztschr f Hyg u Infektionskr* 1948, Apr 1, v 127, Nos 6/8, 501-11 [14 refs]

Canaries were infected with *P. cathemerium*. When parasites appeared in the blood, the birds were treated daily with subeffective doses of mepacrine. The infection was then transferred to two new canaries which were similarly treated, and so on for 27 passages during 10 months. At intervals, the sensitivity of the parasites was compared with those of the original untreated strain. The strain treated with mepacrine never became more resistant to mepacrine than the normal strain, in contrast, there was some evidence suggesting that it might be more sensitive. This work was done during 1944. [WILLIAMSON and LOURIE (this Bulletin, 1948, v 45, 48) found that *P. gallinaceum* did not become resistant to mepacrine when exposed to it *in vivo* for a very long period, it did, however, become resistant to paludrine quite readily.]

F Hawking

BECKMAN, H. Infectivity of Sporozoites of *Plasmodium cathemerium* 3H2 exposed *in Vitro* to Hen and Canary Bloods. *Proc Soc Exper Biol & Med* 1948, Feb, v 67, No 2, 172-6

Previous work had shown that a strain of *P. cathemerium*, maintained since 1937 in mosquito-canary-mosquito passage, was unable to infect the great horned owl, guinea-pig, fowl or man. The present experiments were devised to discover whether chicken's blood was lethal to sporozoites of this species *in vitro*. Heart blood was taken from uninfected canaries and from hens. Clotting was prevented by heparin or sodium citrate and the blood was retained in an incubator at 41.5°C until the sporozoite suspension was ready to seed. The sporozoites were obtained by triturating infected *Culex pipiens* mosquito in Locke's solution and filtering the product through three layers of gauze, the sporozoites appearing in the filtrate. Exactly similar amounts were then added to the canary and hen blood respectively (so that 0.05 cc of the mixture would contain the sporozoites from 1 mosquito). The mixtures were agitated

in the incubator and samples were removed at 30-minute intervals up to 7½ hours, for inoculation into canaries.

The results were clear cut. 78 out of 80 birds inoculated with the parasite in canary blood developed the infection (the incubation period being delayed after the longer exposures in the incubator) while only two out of 8 birds inoculated with the sporozoites in chicken blood subsequently developed the infection. It was thus shown that the blood of the hen exerts an inhibitory action upon the sporozoites of *P. cathemerium* *in vitro*. P. C. C. Gurnham

### TRYPANOSOMIASIS

HORNEY H. E. Report on the Tsetse-Fly Problems of Maputo. In, *Inst. Med. Trop. Lisbon*. 1947 Dec. v 4 313-71 15 figs. on 9 pls. & 1 folding map.

This is the author's final report on the tsetse fly and trypanosomiasis of the Maputo district and is intended to supersede two earlier ones. It deals with trypanosomiasis of cattle and *Glossina brevipalpis*.

Maputo is the most southern district in Mozambique and lies between Swaziland and the Indian Ocean. It is a most important region because of its relationship to Lourenço Marques. The physiography and climate are briefly described: rainfall is usually more than 100 cm. and falls mainly between October and April; approximate temperatures (in C.) are 18 to 33 from October to December 5 to 23 from May to July and from 10 to 21 in April. The vegetation is described in detail and is discussed in its relation to *Glossina brevipalpis* with a short reference to *G. morsitans*.

There are about twelve plant communities grouped into five types: (1) climax (and near-climax) forest and bush, which provides conditions suitable for the breeding of *G. brevipalpis*; (2) tidal swamp vegetation and (3) grassland, both of which are tsetse feeding grounds; (4) acacias, which are sometimes unfavourable to tsetse though this depends on the nature and incidence of bush clumps; and (5) mixed bushland, where if there is a dense population and little stock, *G. brevipalpis* does not occur but if the people have moved away and game has returned, bush clumps exist which are suitable breeding places. More than 400 common woody plants of the district are listed with notes on the kind of plant and type of habitat. Some of these are illustrated by photographs.

*Glossina brevipalpis* occurs throughout a large part of Maputo, but its exact extent is unknown. It has been taken in many places from the Zululand border to a few miles north of the Bela Vista-Changalane road; the greatest numbers were taken along the river itself. The fly is most active after sunset and it is almost certain that it prefers to hunt by night. Pupae are found close to a good feeding ground, in sites which are not exposed to full sunlight and never waterlogged. Such conditions are usually found under a double but not necessarily thick canopy. Release and recapture experiments showed that the species is a very strong flier and flies several kilometres in one night. Some evidence was also obtained of the decline in numbers during the dry season: most were taken between February and May and few in September. Cattle and other domestic animals, as well as game animals, are occasionally attacked during the daytime but this is not the usual way in which *brevipalpis* gets its blood meals. The hippopotamus appears to be the most important and reliable source of food especially when these animals live near evergreen forest or bush which affords resting and breeding sites for the fly.

A trypanosomiasis survey of apparently healthy domestic animals showed that a large proportion of adult animals possess much immunity. Out of



## Trypanosomiasis

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10,880 cattle, 1,256 goats and 31 donkeys, 10-15 per cent of the bovines and 1-83 per cent of the goats were shown to be harbouring trypanosomes, of the positive smears, 67 per cent showed *T. vivax*, 16 per cent *T. congolense* and 17 per cent mixed infections of both. An experiment with *G. brevipalpis* and imported *G. morsitans*, to determine whether the species of tsetse had anything to do with the mildness of the cattle trypanosomiasis in Maputo, left the matter undetermined because of the failure to induce *G. morsitans* to feed. Of the 72 *G. brevipalpis* which fed on infected animals, 50 per cent showed some development of trypanosomes, in 11 flies (15.3 per cent) the labial cavity had been invaded and 4 flies (5.5 per cent) became positively infective with trypanosomes in the hypopharynx.

The mildness of the trypanosomiasis in Maputo is due, in the author's opinion, to the smallness of the herds and to the good and adequate food, and possibly to an acquired immunity reinforced by subsequent infections. Though the existing conditions are far from satisfactory he considers that it would be better not to interfere unless the contact between fly and cattle could be broken completely.

In an attempt to discover whether this could be done, two experimental clearings are being made and studied. In the first, the intention is to turn all bushland into grassland with scattered trees. The second clearing adjoins the first, and here the main object is to attack all breeding sites, to ascertain and afterwards to demonstrate the kind of work which will have to be done outside settled areas in order to permit expansion as more land is required for settlement. At present, each of these areas is less than 1,000 acres, and together they are too small to safeguard the contained animals from *G. brevipalpis*, but they may show that flies caught inside are transitory invaders and if the first clearing can be extended to a full-size settlement protected by a second, it is hoped to show that it is possible to make an area fly-free and prepare it for intensive settlement. The author has been able to supervise only the beginning of this experiment.

In a short reference to *G. austeni* only two foci of this species are described. They are both on the Changalane river where a few flies have been taken. Before economic methods of control can be worked out much more must be known about the distribution and bionomics of this species of tsetse fly.

H S Leeson

FERREIRA F S da C Sobre o grau de infestação por tripanosomas da *Glossina palpalis* da Guiné Portuguesa [The Degree of Infestation of *Glossina palpalis* by Trypanosomes in Portuguese Guinea] *An Inst Med Trop* Lisbon 1947 Dec v 4 91-7 English summary

1 FERREIRA F S da C Relatório do Chefe da Missão de Estudo e Combate da Doença do Sono na Guiné referente a 1945 [Report of the Sleeping Sickness Survey of Portuguese Guinea for 1945] *An Inst Med Trop* Lisbon 1947, Dec v 4 713-49 14 figs (1 map)

II FERREIRA F S da C Relatório do Chefe da Missão de Estudo e Combate da Doença do Sono na Guiné referente a 1946 [Report of the Sleeping Sickness Survey of Portuguese Guinea for 1946] *An Inst Med Trop* Lisbon 1947 Dec v 4 751-89 7 figs (3 maps) & 3 pls

These papers constitute a report of the organization of the campaign and the results of a year's work (1247)

PINTO A. R. O recenseamento dos doentes do sono. (Extracto dos relatórios semestrais referentes ao ano de 1946) (*Sleeping Sickness Survey Half-yearly Reports for 1946*). *An. Inst. Med Trop* Lisbon. 1947 Dec., v 4 791-810 7 figs. (1 map).

This record applies to a part of Portuguese Guinea, depicted in a line map with an area of 45,000 sq. kilometres and a population of 110,000. The people were collected, with the aid of local chiefs, and specimens were taken of gland-juice, blood and cerebrospinal fluid, to confirm suspicious clinical diagnosis, the gland-juice method especially. Between the 1st March and the 31st December 12,443 persons were examined and 48 (113 males and 135 females) were positive. 24 were children under 10 years, 61 between 10 and 20, 159 between 20 and 60 (no subdivision of these decades is given) and 4 over 60 years. The treatment adopted was by antypol and trypanamide. The former was given thus for an adult: First dose 0.5 gm., three days later 1.0 gm., and thereafter 1 gm. weekly to a total of 7.5 gm. The trypanamide was given in weekly injections of 2-3 gm. for ten weeks. The results of treatment and any accidents are not dealt with in this report; they are to be detailed in a later report of treatment. The present account includes copies of the various forms for the keeping of records. *H. Harold Scott*

HOLLINS, C. & LEWIS-FAMING, E. The Sedimentation Rate in the African Patient with special reference to Trypanosomiasis. *Trans. Roy. Soc. Trop. Med. & Hyg.* 1947 Oct., v 41 No. 2, 217-40 3 figs. (14 refs.)

The normal European blood sedimentation rate is less than 5 mm. in 1 hour but the majority of Africans have readings of between 10 mm. and 15 mm. at one hour and most patients suffering from trypanosomiasis have rates above 20 mm. In determining the sedimentation rate the authors mixed 4 parts of blood with one part of 5 per cent. sodium citrate solution, and they found that when the sedimentation rate is extremely rapid, as in cases of trypanosomiasis, a 10-minute reading is largely a measure of the intensity of the agglutination and a 1 hour reading is an approximation to the packed-cell volume. The cause of the high sedimentation rate of the apparently normal African is obscure. Examination of a group of African troops showed that the majority had plasma albumin to globulin rates of about unity whereas those of Europeans average 1.7:1. The authors believe that the difference in the sedimentation rates is associated with this difference in the albumin-globulin ratio, and that the clinical significance of the high African sedimentation rate is an indication of diminished resistance to disease.

In trypanosomiasis the increase in the sedimentation corresponds roughly to the clinical severity of the disease, and in some districts with the changes in the cerebrospinal fluid. It may be that as the sedimentation rate rises with the progression of the disease the rate is high by the time the nervous system is affected, or it may be that when the sedimentation rate is high the nervous system becomes susceptible to invasion. It is suggested that the sedimentation rate is an expression of the equilibrium between the patient's resistance and the virulence of the trypanosome, variation in the patient's resistance being probably a more potent factor in causing change in the sedimentation rate than is variation in the virulence of the trypanosome. In trypanosomiasis a low sedimentation rate indicates an early infection or a long, standing infection of low virulence; a high sedimentation rate probably carries a poor prognosis as it indicates a relatively low resistance on the part of the patient. Trypanocidal therapy rapidly reduces a high sedimentation rate in trypanosomiasis. Consequently, although not replacing proper clinical and laboratory examinations,

determination of sedimentation rates is a valuable auxiliary measure in assessing treatment and in the diagnosis of cryptic infections. During mass surveys sedimentation rates should be determined in all individuals in whom trypanosomes cannot be found. Patients with a high sedimentation rate may then be given a single injection of antrypol or pentamidine and re-examined a month later. Those showing a pronounced fall in sedimentation rate should be regarded as cases of trypanosomiasis.

F Murgatroyd

LAUNOY, L. Essai sur la chimio-prévention, par voie orale, chez le rat, de l'infection expérimentale à *Trypanosoma gambiense* [souche Yaoundé] (Note préliminaire) [Chemoprophylaxis by the Oral Route against the Yaoundé Strain of *T. gambiense* in the Rat] Reprinted from *Ann Pharm Françaises* 1947, Dec, v 5, 599-605

The Yaoundé strain of *T. gambiense* has neurotropic properties in mice and rats [ROUBAUD and PROVOST, this Bulletin, 1942, v 39, 234, STÉFANOPOUL and ÉRÉVÉ, *ibid*, 1945, v 42, 258, ROUBAUD, STÉFANOPOUL and DUVOLON, *ibid*, 1946, v 43, 419]. The neurotropic effects are somewhat more pronounced in mice, in which the most striking feature is paralysis of the hind limbs, than in rats, which exhibit somnolence, irritability, tremors, loss of sphincter-control and sometimes paralysis.

The authors have found the incubation period of this strain in rats to average 22-23 days and the total duration of infection to vary widely around a mean of about 65 days. Previous workers with this strain in rats have found that trypanosomes are only occasionally to be seen in the blood, and then only in small numbers, a terminal septicaemia being very infrequent. LAUNOY finds now, however, that two types of infection are of most common occurrence, as follows: (a) Parasites slowly increase to a fairly high count, and there are then several waves of alternate trypanolysis and re-accumulation of parasites, which are frequently present in more or less great number, and can be seen until death for more than a month. They may continue to be scanty or absent up to the time of death. This type of infection is usually more chronic than type (a).

Prophylactic experiments were carried out with "Lomidine", which is the 2, 2'-methylene-bis-hydroxynaphthoate of pentamidine base, administered orally. This preparation is insoluble in water, but is apparently absorbed in the intestinal tract. Doses of 0.15-0.3 gm per 100 gm body weight were given orally, and a heavy suspension of trypanosomes was then inoculated intraperitoneally 1 to 8 days later, in 17 rats, with an equal number of controls. In another experiment the dose was 0.2 gm per 100 gm body weight, with a period of 4 weeks between treatment and inoculation, but there were only 2 rats, with 1 control, in this particular experiment. All the untreated rats became infected in the usual way, but those treated prophylactically remained free of infection within observation periods which varied up to about 285 days.

E M Lourie

LAUNOY, L & LAGODSKY, H. Sur la prophylaxie chimique de quelques trypanosomoses animales expérimentales [Chemoprophylaxis of some Experimental Trypanosome Infections] Reprinted from *Ann Pharm Françaises* 1946, Mar-Apr-May, v 4, 97-8

The following figures are given for the curative and prophylactic effect of pentamidine, administered subcutaneously to rats [See also LAUNOY & LAGODSKY, this Bulletin, 1947, v 44, 702]

Infection	Dose in mgm./100 gm. body weight	
	Curative	Protective (25-30 days)
<i>T. cruzi</i>	0.5	2.0
<i>T. equiperdum</i> .. ..	0.7-0.9	2.0-2.5
<i>T. n. n.</i> .. ..	7.0-9.0	25.0

E. M. LORIE

PIFANO C., F. MAYER, M., MEDINA, R. & BENAVIDES PINTO H. Primera comprobación de *Trypanosoma rangeli* en el organismo humano por cultivo de sangre periférica. [First Demonstration of *Trypanosoma rangeli* in the Human Body by Cultivation of the Peripheral Blood.] *Archivos Venezolanos de Patol. Trop. y Parasit. Med.* 1948, Jan. v. 1 No. 1: 1-31, 8 figs. (13 refs.) English summary.

Since the discovery by TEJERA in 1920 (this Bulletin 1921 v. 17: 97) of *Trypanosoma rangeli* in the gut of one of the vectors of Chagas's disease *Rhodnius prolixus* from Venezuela, it was suspected that this parasite had a vertebrate host as well. It was subsequently reported, alone or in association with *T. cruzi* from Triatomid bugs of Uruguay, Colombia and Venezuela. The recent finding of *T. rangeli* together with *T. cruzi* in laboratory-bred *R. prolixus* fed on a patient suffering from Chagas's disease seemed to indicate that the first named trypanosome was a human parasite (DIAS and TORREALBA, 1943; this Bulletin 1944 v. 43: 108). Its presence in two other patients from Venezuela was also demonstrated by xenodiagnosis by MEDINA (unpublished) and finally in the present paper the authors record the successful isolation of *T. rangeli* in culture (N.N.V. medium) of the blood from a girl, aged 12, in Venezuela. The patient was suspected to be suffering from Chagas's disease but cultures revealed only developmental stages of *T. rangeli* corresponding to those found in *Rhodnius*. All attempts to infect various animals (rodent, cat, lizards, fowls) have so far failed.

The greater part of this paper is devoted to a detailed description of the stages of development of *T. rangeli* in culture and in the bug. In the latter the flagellates occur throughout the alimentary tract and are represented by long and short tritrichid forms and by slender trypanosomes measuring on the average 41  $\mu$  and 43-6  $\mu$  in length respectively. Similar forms are found in cultures. The flagellates differ from the corresponding forms of *T. cruzi* in the minute size of the kinetoplast and in other structural features which are evident in the numerous figures illustrating the paper. C. A. HARRIS

DIAS E. Importancia continental da doença de Chagas. [Importance of Chagas's Disease in South America.] *Brazil-Medico* 1948 June 5 & 12, v. 62, Nos. 23/24: 17-19. (12 refs.)

The author has brought together recent figures showing the prevalence of Chagas's disease and of the vectors of *T. cruzi* in different countries of South America. From a small zone of Bambuí more than 65,000 of the bugs were sent to the Oswaldo Cruz Institute in the space of 4 years and 14,750 from 13 huts. Cardiac lesions are common and serious: they were present in about half the chronic cases in Minas Gerais and in 95 per cent of these there were signs of interference of conduction of all grades in nearly half blockage of the

right ramus Sudden death from these heart conditions is common. The extent of spread of infection is evidenced by the fact that among 144 students of Tucumán, Santiago del Estero and Catamarca, 23.7 per cent were positive by xenodiagnosis and 30 out of 72 gave a positive fixation of complement.

In Uruguay many hundreds of acute cases have been reported and TÁLICE stated in 1939 that there were 4,000-5,000 acute cases there every year. In Paraguay not many cases have been recorded but they are probably fairly numerous because infected transmitters are common in the rural dwellings. In Chile, infection was found in 40 per cent of 9,000 triatomas examined and 31.8 per cent of 1,445 sera of rural inhabitants gave positive complement fixation reactions. In Bolivia, 54.3 per cent of 791 vectors examined were infected and 12.6 per cent of 961 xenodiagnostic tests were positive, as were sera of 23 out of 74 examined. In Venezuela nearly half (48.8 per cent) of 3,429 specimens of *Rhodnius prolixus* were positive according to MEDINA, DAS in 1945 found 56.3 per cent positive among 2,802, and PIFANO 76.2 per cent of 1,735 examined. Other places are mentioned but only in general terms, thus, in Panama "scores of cases and several fatal", in French Guiana "it is well known that infected transmitters are present and also that there are cases of infection", DAVIS and SULLIVAN found 1,909 positive results to complement fixation in Texas [the total examined is not stated].

H Harold Scott

DE FREITAS, G & DE CASTRO, F T Cultura de *S. cruzi* em meio autoclavável, isento de células e proteínas precipitáveis (Nota preliminar) [Culture of *Trypanosoma cruzi* in an Autoclaved Medium, free from Cells and Coagulable Proteins] Hospital Rio de Janeiro 1948, May, v 33, No 5, 725-30

The English summary appended to the paper is as follows —

"(1) The authors demonstrate that fresh blood can be substituted by an enzymatic digest of lyophilized blood, in supporting the growth of '*S. cruzi*'.

"(2) A new liquid medium (DP-30) for '*S. cruzi*' is presented, free from cells, particles and coagulable proteins and sterilisable by autoclave.

"(3) The medium is basically composed of a peptic digest of blood, tryptic peptone and dextrose. Full details on the preparation are given in the developed text.

"(4) Twenty-five transfers have been obtained until the publication of this note, without any sign of decrease of the multiplication capacity of the organism.

"(5) Some preliminary counts revealed 8,000,000 individuals per cc in tubes with 4 cc of medium and inoculated with 25 per cent of a culture. With large inocula, (50%) approximately 12,000,000/cc can be obtained in flasks with 100 cc of medium.

"(6) The culture can be done in tubes for maintaining the samples or in Erlenmeyer flasks for large scale production."

FLOCH H & CAMMIN R Deux nouveaux cas de maladie de chagas en Guyane française [Two New Cases of Chagas's Disease in French Guiana] Bull Soc Path Exot 1948 v 41 Nos 5/6 347-50

BRUMPT L C Trois cas de maladie de chagas avec présence de cellules de Mott dans le sang [Three Cases of Chagas's Disease with Mott Cells in the Blood] Bull Soc Path Exot 1948 v 41 Nos 5/6 350-53

POUNT, L. La cardiopatía crónica de la enfermedad de Carlos Chagas. [Chronic Cardopathies in Chagas's Disease.] *Revista Méd. Urubana*. 1948 June 4 v. 35 No. 23 1075-88. [57 refs.]

The author gives an account of and discusses 73 cases of Chagas's disease from the point of view of the cardiac conditions they were seen in the Medical Faculty of the University of Bahia, Brazil. The diagnosis in each case was made by complement fixation with the Davis antigen or by xenodiagnosis, in many instances by both methods. Examination of the heart was made in 40 of the patients by physical, radiographical and electro-cardiographic means. In 32 (written of as 80 per cent.) there was interference of propagation of the stimulus, auriculo-ventricular or intraventricular and in 23 (57.5 per cent.) disturbance of the start of the stimulus and in 47.5 per cent. (19 cases) alteration of rhythm.

In more detail partial A-V block was found in 8 patients, total in 11. I-V block of the right ramus in 19 none of the left. Primary changes of the ST and T in 25, ventricular extrasystoles in 22, auricular in 4 supraventricular paroxysmal tachycardia in 1.

In an extensive table are shown the clinical manifestations—subjective and objective signs, arterial pressure, the Wassermann, Kahn or Hime reactions—the X-ray findings and the electrocardiogram of each of the 40 patients. (The preparation of this article must have entailed much work and study to which no mere abstract can do justice. Close study of the details is needed by those interested to appreciate the heart lesions of Chagas's disease.)

|| Harold Scott

MOULDER, J. W. Chagas in the Glucose Metabolism of *Trypanosoma lewisi* during the Course of Infection in the Rat. *J. J. med. Dis.* 1948, July-Aug., v. 83, no. 1 42-9. 5 figs. [17 refs.]

MOULDER, J. W. The Oxidative Metabolism of *Trypanosoma lewisi* in a Phosphate-Saline Medium. *J. J. med. Dis.* 1948, July-Aug. v. 83, no. 1 32-41. [Refs. in footnotes.]

## LEISHMANIASIS

WILNER, P. R. & HARDICKE, T. A. Relapsing Kala-Azar. Report of a Case with Cure effected by Stilbamidine. *New England J. J. Med.* 1948 Aug 1, v. 239 No. 7 50-53, 5 figs. [12 refs.]

"A case of kala-azar is reported. Difficulties in diagnosis were encountered emphasizing the varied nature of the disease. The patient relapsed after two courses of neostibosan. Complete cure was obtained with 4.325 gm. of stilbamidine. It is suggested that kala-azar be included in the differential diagnosis of any obscure febrile illness. Stilbamidine may be considered efficacious in relapsing visceral leishmaniasis until better toxic drugs have been proved to be of value.

GRVA, A. & BINAGHI, G. Alterazioni cardio-circolatorie nei bambini affetti da leishmaniosi viscerale. Cardiovascular Changes in Children with Visceral Leishmaniasis. *Chir. Pediatr.* 1947 Sept. v. 21 No. 9 534-47. 3 figs. [27 refs.]

The authors have examined 1 children their ages ranging between 17 months and 14 years suffering from infantile kala-azar. For each of these they have noted the systolic and diastolic arterial pressure the venous pressure

the pulse and respiration rates, the red and white cell counts, the haemoglobin and the electrocardiogram. The details recorded differ within fairly wide limits, particularly the blood-cell counts. The red corpuscles ranged between just over 1 million and over 4 millions, and the white corpuscles between 2,800 and 10,200 per cmm. Generally, the arterial pressure [presumably the systolic] was a little below the normal and the pulse tended to be more rapid, owing in large part at least to the anaemia present. The PQ interval was usually increased, and, taken in association with the tachycardia, is to be interpreted as a retardation of the atrio-ventricular conduction. In one only was there respiratory arrhythmia and in none was extrasystole seen. In brief, the electrocardiogram shows no valid evidence of change which can be regarded as characteristic of leishmaniasis, but merely as indicating myocardial affection which may result from a toxic factor or the anaemia present, and the absence of its modification after injection of atropine does away with the hypothesis that the blockage is of a "nervous character".

H Harold Scott

### FEVERS OF THE TYPHUS GROUP

WEYER, F, FRIEDRICH-FREKSA, H & BERGOLD, G. Die Beziehungen der Rickettsien zu Bakterien und Viren [The Relationships of Rickettsiae to Bacteria and Viruses] Reprinted from *Die Naturwissenschaften* 1944, Nov-Dec, Nos 44/52, 361-5, 6 figs [10 refs]

This paper is illustrated by six photographs of *Rickettsia mooseri*, five were taken with the electron microscope at a magnification of 40,000 diameters, and one with dark-background illumination at a magnification of 1,000 diameters. The technique employed is described.

The authors claim that the findings indicate clearly the absence of relationship between rickettsiae and the elementary or polyhedral bodies of viruses. On the other hand rickettsiae resemble bacteria in having a rounded form and a definite internal structure, they multiply by fission, are insoluble in weak solutions of NaOH, and contain a polysaccharide related to that of *Proteus X* strains, as is shown by the Weil-Felix reaction.

John W D Megaw

GIROUD, P & VARGUES, R. Diminution du nombre de rickettsies virulentes par dessiccation [Reduction caused by Desiccation in the Number of Virulent Rickettsiae] *C R Soc Biol* 1948, Apr, v 142, Nos 7/8, 438-40

Suspensions were made from the lungs of mice heavily infected with epidemic typhus rickettsiae, half of each was kept at  $-24^{\circ}\text{C}$  to serve as a control, the rest was desiccated by three different methods (1) Over calcium chloride *in vacuo* at  $15^{\circ}\text{C}$ , (2) Lyophilization by the method of Flosdorff and Mudd, and (3) Lyophilization by the method of McFarlane, in which the suspension is kept at a temperature of  $-16^{\circ}\text{C}$  till desiccation is complete.

The virulence of the three products was estimated by Giroud's rabbit intradermal test, four different dilutions of each product were injected into one flank of a rabbit and four corresponding dilutions of the control suspension were injected into the other flank. An arbitrary standard, based on the diameter and thickness of the resultant skin swellings, was adopted. The reduction in virulence of the first product was estimated as being 1,000 to 1, of the second it was 100 to 1, and of the third, 10 to 4.

The three products when inoculated intraperitoneally into guinea-pigs, and when tested for their power of fixing the agglutinins of an immune serum, showed little difference in their activity.

[Doubts may be felt as to whether the extent of the skin reaction constitutes a true index of the number of virulent rickettsia surviving in each product.]

John W. D. McGraw

DI MITRESCO N. CONSTANTINESCO S. BOTEZ V. & STURDZA N. Contribution à l'étude sérologique du typhus exanthématique. [A Contribution to the Serology of Exanthematic Typhus.] *Arch. Roumaines Path. Exp. et Microbiol.* 1945-1946-1947 v. 14 No. 1/4 113-35. (18 refs.)

The authors describe a technique by which they claim to have obtained consistently definite results in a survey of the incidence of Weil-Felix reactions among the inhabitants of various villages of Rumania in which outbreaks of typhus had occurred or were occurring.

The percentage of positive titres between 1:200 and 1:400 was 31.1 in persons who had been attacked within the previous year; it was 10.3 among those who had been in direct contact with infected persons; 8.1 among other persons in the villages, and only 3.7 among the inhabitants of unaffected villages. No higher titres were observed among persons not actually suffering from the disease. Every patient had a titre above 1:400 and the occurrence of titres of 1:1,000 or over was regarded as evidence of the presence of the disease in a village.

Among persons vaccinated with the Weigl or Cox type of vaccine the highest titre observed was 1:250.

John W. D. McGraw

GIRLOUD P. & LE GAC P. Parenté sérologique de la fièvre boutonneuse et du typhus épidémique. [The Serological Relationship between Boutonneuse Fever and Epidemic Typhus.] *C. R. Acad. Sci. Paris* 1948 Apr. 142 No. 78 436-8.

Rickettsia-agglutination test against murine and epidemic rickettsiae was carried out on the sera of 11 patients suffering from boutonneuse fever contracted in France. Reactions against epidemic rickettsiae occurred at titres of 1:160 or over in seven patients, and in four of these cases there were also positive reactions though at lower titres against murine rickettsiae.

Weil-Felix tests were carried out on seven of the patients; four reacted with *Proteus OX19* at titres of 1:100 or over; two of these reacted also with *Pr. OX* and one with *P. OXA*.

The authors conclude that there is an antigen common to epidemic typhus and boutonneuse fever which could explain certain points that are still obscure in our knowledge of the typhus fevers.

John W. D. McGraw

COMBESCO D. Séro- et chimiothérapie dans le typhus exanthématique expérimental chez le cobaye. [Serum Therapy and Chemotherapy of Experimental Typhus in Guinea-pigs.] *Arch. Roumaines Path. Exp. et Microbiol.* 1945-1946-1947 v. 14 No. 1/4 231-4.

A brief preliminary note stating the results obtained from experiments to be described in a later paper.

John W. D. McGraw

LEY H. L., JR., SMADKE, J. E. & CROCKER, T. T. Administration of Chloromycetin to Normal Human Subjects. *Proc. Soc. Exper. Biol. & Med.* 1948, May v. 68, No. 1 9-12, 2 figs.

Courses of chloromycetin were given by the mouth to three healthy medical men as a preliminary to a trial of the drug on typhus patients.



The levels of the drug in the blood and urine were tested by a modification of a method devised by JOSLYN and GALBRAITH and personally communicated by them to the authors, this is based on the inhibition of the growth of *Shigella sonnei*

Initial doses of 1.0 gm followed by a ten-days' course of 1.0 gm daily in five divided doses were given to two of the volunteers

In a second test initial doses of 2.0 gm followed eight hours later by single doses of 0.5 gm were given. Appreciable amounts of the drug were detected in the blood within 30 minutes of the first dose, excretion was rapid and no ill effects were detected by examination of the blood and urine or by the volunteers themselves

John W. D. Megaw

SMADEL, J. E., LÉON, A. P., LEY, H. L., Jr & VARELA, G. Chloromycetin in the Treatment of Patients with Typhus Fever. *Proc Soc Exper Biol & Med* 1948, May, v 68, No 1, 12-19, 6 figs

Five typhus patients in a hospital in Mexico D F were treated with chloromycetin by mouth under close expert observation. Three of the patients were adults suffering from epidemic typhus and two were children, one of whom had epidemic typhus and the other had murine typhus. The differential diagnosis was based on rickettsia-agglutination and complement-fixation tests, the former of which in four of the five cases and also in three of six untreated cases became positive several days earlier than the latter.

The detailed case reports suggest that the drug may have been beneficial, but the authors are cautious in their conclusions, which are that the drug is relatively safe and that the effects were sufficiently encouraging to justify further tests.

The dosage suggested is an initial dose of 40 mgm per kilo of body weight followed by a total daily dose of 35 mgm per kilo given in divided two-hourly doses till improvement is noticed and then by a maintenance total daily dose of 20 mgm per kilo given in divided amounts every four hours till the 13th or 14th day after the onset

John W. D. Megaw

ORTIZ MARIOTTE, C. Vacuna profiláctica contra el tifo. prueba de campo [Prophylactic Anti-Typhus Vaccine, a Field Test]. *Bol Oficina Sanitaria Panamericana* 1948, Apr, v 27, No 4, 330-41. English summary

A field test was carried out in strictly controlled conditions in three rural areas of South Mexico. The vaccine used was of the bivalent, Castañeda type containing four parts of murine rickettsiae and one part of epidemic rickettsiae. Among 234 vaccinated persons there were 15 attacks of clinical typhus [apparently louse-borne] and among 214 comparable controls there were 18 attacks. The average severity of the attacks in the vaccinated group was considerably less than in the controls, 17 of the control patients had "severe" or "average" attacks whereas only 6 of the vaccinated fell into these grades.

Although the difference in severity is regarded as statistically significant the authors regard the figures as too small to justify final conclusions.

The trial was carried out in 1942-1943, and the authors mention that an improved vaccine has given good results among persons specially exposed to the risk of infection since 1945

John W. D. Megaw

SAVOOR, S. R., VAHIA, N. S. & SOMAN, D. W. Typhus in Bombay. Part III. Identification of Strains. *Indian Med Gaz* 1948, Feb, v 83, No 2, 70-74 [15 refs]

Strains identified as *Rickettsia mooseri* were isolated from the blood of five patients in Bombay, by mouse inoculation. With simultaneous guinea pig

inoculation only three of the strains were isolated, and as the spleen and brain of infected mice remained infective to guinea-pigs for at least two months the mouse is regarded as the animal of choice for recovering and maintaining infection.

All the strains were orchitic and in other respects gave reactions regarded as indicating a murine type of infection.

A similar strain was isolated from a pooled suspension of the brains of four rats from a house in which a case of the disease had occurred—pools made from the brains of 19 other rats from this house were not infective.

One of the human strains was transmitted, from guinea-pig to guinea-pig from rat to rat and from mouse to mouse by the bites of *Xenopsylla cheopis*.

One strain was maintained in rats for 20 successive passages.

Each of the three strains tested caused complete cross immunity in guinea-pigs against the other two strains but guinea-pigs convalescent from the infection were still susceptible to the Wilmington strain of murine rickettsiae, though only two of the five guinea-pigs tested developed a acrotal reaction. On the other hand the Wilmington strain caused complete immunity against the Bombay strains, which, therefore were regarded as being of lower virulence.

Complement-fixation tests were not carried out and doubts are expressed on the reliability of this reaction—it is stated that a murine strain similar in every respect to the Bombay strains was isolated from a patient in Mysore whose serum had been tested by TOEFIX and had been regarded by him as giving a fixation reaction indicating a closer relationship with Rocky Mountain spotted fever than with murine typhus.

[The occurrence of this conflict in evidence makes it all the more desirable to carry out complete serological tests.]

John H. D. Megan

BALTESCU, I. & CONSTANTINESCU, N. [See one down the rickettsiae murine 'A New Murine Rickettsial Infection.' Arch. Roumains Path. Expt. et Microbiol. 1945-1946-1947 v. 14 No. 1-4 136-85 15 figs. & 7 pls (1 coloured)] (11 refs.)

In a long paper the authors describe an exhaustive investigation of a murine strain of rickettsiae isolated by inoculating guinea-pigs with a pooled suspension of the brains of four rats trapped in Jassy Rumania. One of the rats had a Weil-Felix reaction at a titre of 1-600. The strain was regarded as intermediate between epidemic and murine rickettsiae. It caused an intense febrile and tissue reaction in guinea-pigs but was non-orchitic. In the earlier transfer through guinea-pigs brain substance alone was used as the inoculum and there was a considerable falling off in virulence, but when blood or spleen-suspension was used the virulence at once became greater and it remained constantly high through the rest of the series of 63 transfers. Transfer through a rat also caused an increase in the virulence of the attenuated strain—this had become non-infective to mice but by the 20th passage the brain and spleen of infected mice caused a sharp febrile and orchitic reaction in guinea-pigs.

Rabbits, dogs, and spermophiles were susceptible but cats resisted attempts at infection.

A human volunteer was inoculated subcutaneously with brain substance of the guinea-pig of the 1st passage and developed a febrile attack lasting 1 day, there was a papular rash, and the Weil-Felix reaction was positive in rising titre which reached 1-400 by the end of the attack.

Another volunteer was inoculated with brain and spleen suspension from a guinea-pig of the 42nd passage. He had an inapparent reaction, detected only by the isolation of rickettsiae from the blood. Three other persons inoculated in the same way from guinea-pigs of various passages did not react.

The spermophile, *Citellus citellus*, harboured infection for at least 40 days in its brain and spleen and was regarded as the animal of choice for maintaining the strain. There was no cross-immunity with epidemic-typhus rickettsiae. Many other observations were made but there is no mention of complement-fixation or rickettsia-agglutination tests.

John W D Megaw

LIU, Wei-T'ung, WANG, Pe'i-Jen & CHING-CHANG, Hwei. Typhus-like Fever of *Proteus vulgaris* OXK Type in Northwest China. Report of Six Cases. *Chinese Med J* Shanghai 1948, Mar, v 66, No 3, 130-40 [23 refs]

Six cases are described in which the *Proteus* OXK type of Weil-Felix reaction occurred at titres of 1-160 to 1-640, one of the patients reacted against *Pr* OX19 at a titre of 1-80, all the others were negative with *Pr* OX19 and *Pr* OX2.

In four of the cases complement-fixation tests against epidemic-typhus antigens were carried out, three were negative, but one reacted at a titre of 1-1,024 though his serum did not agglutinate *Pr* OX19 or OX2.

Among 353 normal persons in the area only two gave an OXK reaction (at a titre of 1-80), and among 37 typhus patients only three gave OXK reactions, at titres ranging from 1-80 to 1-320.

In view of the above and other considerations the authors conclude that the cases "might represent a disease closely related to, if not identical with tsutsugamushi disease".

Five of the patients were residents of Lanchow, situated on the Yellow River which periodically floods the city and its suburbs.

It is stated that FAUST in 1923 found organisms, which he regarded as resembling *Rickettsia moppo*, in spleen sections from two patients in Wuchang and that he suggested the possible occurrence of tsutsugamushi disease in the lower Yangtse Valley. Apart from this the only previous evidence of the occurrence of the disease in China is said to be the recent finding by Wei of typhus cases of the *Pr* OXK type in Kunming in South-West China.

John W D Megaw

KELSEY, W M & HARRELL, G T. Management of Tick Typhus (Rocky Mountain Spotted Fever) in Children. *J Amer Med Ass* 1948, Aug 14, v 137, No 16, 1356-60, 3 figs [Refs in footnotes]

The authors point out that tick typhus is now more prevalent in some Eastern States than in the Rocky Mountain area which till recent years was regarded as the only part of the world in which the disease occurred. In 1945 only two cases were reported from Montana, and six from Idaho, whereas 99 were reported from Virginia and 57 from North Carolina. The case-mortality rate in North Carolina during 1944 and 1945 was nearly 32 per cent.

The present paper deals with 27 cases among children, there were seven deaths, but this high mortality rate is attributed to the fact that most of the patients were sent to hospital because their condition was critical.

Only 50 per cent of the patients were known to have been bitten by a tick shortly before the onset. With the Weil-Felix test the highest titres observed were the *Proteus* OX19, though in one patient who died the OX2 and OXK strains gave higher titres. The complement-fixation test was indicative of tick-borne infection though three patients gave reactions against murine rickettsiae, but in each case at a lower titre.

Treatment with hyperimmune rabbit serum was tried in some cases, among the six patients whose treatment was started within three days of the onset there was no death, but two patients treated from the 5th day onwards died, and the mortality in the serum-treated group as a whole was 25 per cent.

The general treatment was supportive the authors believe that several patients were saved who otherwise would have died. A high intake of proteins and vitamins was maintained.

In the discussion one speaker rebuked the authors for using the name tick typhus he said that this name would apply equally to boutonneuse fever which was a different disease. The senior author defended the name on several grounds especially because the name Rocky Mountain spotted fever had misled many practitioners by suggesting that the disease was limited to a geographical region and because the name tick typhus correlates the disease with the vector just as happens with the names louse borne typhus and murine typhus.

John H. D. Morgan

COMBESCO D. Sur une épidémie de fièvre boutonneuse observée à Constantza-Roumanie. (Deuxième-mémoire.) [An Epidemic of Boutonneuse Fever observed at Constantza (Rumania).] Arch. Roum. Sci. Path. Exp. et Microbiol. 1945-1946-1947 v. 14 No. 14 89-112, 8 charts. [46 refs.]

This paper is a much delayed continuation of a memoir published in 1932. It deals with an epidemic of boutonneuse fever in which 34 cases were observed in Constantza in the summer of 1931. The author now describes the isolation in September 1933, of rickettsiae from ticks (*Rhipicephalus sanguineus*) collected from dogs in Constantza. Inoculated guinea pigs sometimes developed a scrofula reaction. There was no cross immunity between the rickettsiae and those of epidemic typhus.

John H. D. Morgan

## YELLOW FEVER

ELLIS G. M. John Williams and the Early History of Yellow Fever. Brit. Med. J. 1948, Sept. 4 474-6 [14 refs.]

MARTY A. F. The Epidemiology of Yellow Fever. J. Roy. San. Inst. 1944 Sept. v. 68, No. 3 534-8. [14 refs.]

CAUSBY O. R. & HUMM H. W. Dispersion of Forest Mosquitoes in Brazil. Preliminary Studies. Amer. J. Trop. Med. 1948, May v. 28 No. 3 469-80 2 figs.

Two experiments with forest mosquitoes were made in the Passos region in Minas Gerais, Brazil from April to June 1947 during an investigation into the rôle of these mosquitoes in the dispersion of yellow fever. The object of the first experiment was to determine whether marked mosquitoes could be recaptured and whether they remained localized or left the point of liberation. 1,670 *Haemagogus spegazzini* and 803 *Aedes leucocelarius* and 8,752 specimens of other sylvan species were therefore marked and released. During fifteen of the following seventeen days 2,074 (18.3 per cent) mosquitoes were recovered. The percentages of recaptures were of *H. spegazzini* 9-20, of *Aedes leucocelarius* 50-60 and of the other species 16-7. Almost half were taken at the point of release and others in the neighbouring forests. 3 *H. spegazzini*, 10 *Aedes leucocelarius* and 27 others were found in a forest one kilometre from the release point beyond an intervening open pasture. Most were recovered during the first four days: the last *H. spegazzini* on the fifth day and the last *Aedes leucocelarius* on the twelfth day.

The second experiment was designed to discover the usual flight range of forest mosquitoes. The above-named species were not available in large numbers but other species were common. Among the released species were *Aedes serratus* (6,598), *Aedes scapularis* (2,879), *Taeniorhynchus chrysotum* (6,876) and *T. fasciolatus* (6,019). In all 31,689 mosquitoes of sixteen species were used. Recaptures were made on twenty-five days during a thirty-day period 614 at the point of release and 29 in 11 of 28 outlying forests. Species recaptured 800 metres or more from the release point were *Aedes serratus* (16), *Aedes scapularis* (5), *Aedes crumifer* (1), *Psorophora ferox* (4), *Anopheles* sp (2) and *Chagasia fajardo* (1). *Aedes serratus* was recaptured in the greatest distance and over the longest time (25 days), it was also found at the greatest distance (4.7 kilometres). *Aedes scapularis*, an experimental vector of yellow fever, was recovered at a distance of more than 4 kilometres, and 11 days after release.

H S Leeson

DE AZEVEDO, J F, CAMBOURNAC, F J C & PINTO, M R. Resultados de um inquérito sobre febre amarela na Guiné Portuguesa [Results of a Yellow Fever Survey in Portuguese Guinea] *An Inst Med Trop* Lisbon 1947, Dec, v 4, 17-24. English summary.

"1 The authors carried out a survey on the presence of yellow fever in the territory of the Portuguese Guinea by using mouse protection tests made with blood sera from indigenous people.

"2 The sera were collected in most of the regions of the territory and in the people of all localities visited there were some sera which gave positive mouse protection tests.

"3 Positive results have been found with sera from people between 7 and 70 years of age.

"4 As previous to the survey mass vaccination against yellow fever had been started in almost all the regions of the territory, it is possible that at least some of the positive tests were due to the prophylactic inoculations.

5 In one locality in which no prophylactic inoculations had been performed, it was observed a positive test with a serum from a person 70 years old, which is the proof that at least in the past there were cases of yellow fever in that region.

"6 As the number of the tests made is small and possibly most of the people observed had been inoculated previously with yellow fever vaccine, it is not possible to draw definite conclusions about the presence of the disease in the territory of the Portuguese Guinea except for one locality as mentioned above.

"7 As it is also possible that some of the positive tests may indicate cases of yellow fever, it is advised to continue with the prophylactic measures already started and that all the people coming from outside the territory should be inoculated against yellow fever."

## DENGUE AND ALLIED FEVERS

PAUL J R MELNICK, J L & SABIN, A B. Experimental Attempts to transmit *Phlebotomus* (Sandfly, Pappataci) and Dengue Fevers to Chimpanzees. *Proc Soc Exper Biol & Med* 1948 Mar, v 68 No 1, 193-8. 3 figs. [10 refs.]

Sandfly fever virus contained in human blood samples from Cairo was inoculated subcutaneously and intracutaneously into six chimpanzees. The

The general treatment was supportive. The authors believe that several patients were saved who otherwise would have died. A high intake of proteins and vitamins was maintained.

In the discussion one speaker rebuked the authors for using the name tick typhus. He said that this name would apply equally to boutonneuse fever which was a different disease. The senior author defended the name on several grounds, especially because the name Rocky Mountain spotted fever had misled many practitioners by suggesting that the disease was limited to a geographical region, and because the name tick typhus correlates the disease with the vector just as happens with the names louse-borne typhus and murine typhus.

John W. D. Megaw

COMBESCO D. Sur une épidémie de fièvre boutonneuse observée à Constanța Roumanie. (Deuxième-mémoire.) [An Epidemic of Boutonneuse Fever observed at Constanța (Rumania).] Arch. Roum. sci. Path. Expér. et Microbiol. 1945-1946-1947 v. 14 No. 1/4 89-111, 8 charts. [46 refs.]

This paper is a much delayed continuation of a memoir published in 1932. It deals with an epidemic of boutonneuse fever in which 34 cases were observed in Constanța in the summer of 1931. The author now describes the isolation in September 1933, of rickettsiae from ticks (*Rhipicephalus sanguineus*) collected from dogs in Constanța. Inoculated guinea-pigs sometimes developed a scrub reaction. There was no cross immunity between the rickettsiae and those of epidemic typhus.

John W. D. Megaw

## YELLOW FEVER

FADLEY G. M. John Williams and the Early History of Yellow Fever. Brit. M. J. 1948, Sept. 4 474-B. [14 refs.]

M. HARRY A. F. The Epidemiology of Yellow Fever. J. Roy. San. Inst. 1948, Sept., v. 68, No. 3 334-B. [14 refs.]

CALVIN O. R. & KUMM H. W. Dispersion of Forest Mosquitoes in Brazil. Preliminary Studies. Amer. J. Trop. Med. 1948, May v. 29 No. 3 469-80 + figs.

Two experiments with forest mosquitoes were made in the Passos region in Minas Gerais, Brazil from April to June 1947 during an investigation into the rôle of these mosquitoes in the dispersion of yellow fever. The object of the first experiment was to determine whether marked mosquitoes could be recaptured and whether they remained localized or left the point of liberation. 1,670 *Haemagogus spegazzinii*, 903 *Aedes limicola* and 8,752 specimens of other sylvan species were therefore marked and released. During fifteen of the following seventeen days 2,074 (18.3 per cent) mosquitoes were recovered. The percentages of recaptures were of *H. spegazzinii* 9.2, of *Aedes limicola* 50.6 and of the other species 18.7. Almost half were taken at the point of release and others in the neighbouring forests. 3 *H. spegazzinii*, 10 *Aedes limicola* and 27 others were found in a forest one kilometre from the release point beyond an intervening open pasture. Most were recovered during the first four days: the last *H. spegazzinii* on the fifth day and the last *Aedes limicola* on the twelfth day.

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H S Leeson

DE AZEVEDO, J F, CAMBOURNAC, F J C & PINTO, M R. Resultados de um inquérito sobre febre amarela na Guiné Portuguesa [Results of a Yellow Fever Survey in Portuguese Guinea] *An Inst Med Trop* Lisbon 1947, Dec, v 4, 17-24. English summary

"1 The authors carried out a survey on the presence of yellow fever in the territory of the Portuguese Guinea by using mouse protection tests made with blood sera from indigenous people

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## DENGUE AND ALLIED FEVERS

PAUL, J R MELNICK, J L & SABIN A B. Experimental Attempts to transmit *Phlebotomus* (Sandfly, Pappataci) and Dengue Fevers to Chimpanzees. *Proc Soc Exper Biol & Med* 1948 May, v 68, No 1, 193-8, 3 figs [10 refs]

Sandfly fever virus contained in human blood samples from Cairo was inoculated subcutaneously and intracutaneously into six chimpanzees. The

only reactions observed were short attacks of fever and listlessness in the two animals which allowed their temperature to be taken.

The incubation period was five days and the fever lasted about six days in both cases. In one animal the chart shows two humps spaced about four days apart and in the other the fever curve appears to be of the "saddle-back" type. No conclusion was reached regarding the susceptibility of the animals.

Nine chimpanzees were inoculated with strains of dengue virus contained in serum taken three years earlier from human volunteers and kept in a box containing solid  $\text{CO}_2$ . The temperature of five animals could be recorded each of the charts shows a slight rise of temperature between the 5th and 10th day after inoculation, and a second slight rise between the 12th and 14th day. Mouse-neutralization tests showed the complete absence of antibodies before inoculation and the presence of abundant antibodies 54 days after inoculation. There was therefore evidence of the occurrence of an inapparent infection.

John B. D. Macfar

MELNICK J. L., CURRY F. C. & SARKIS A. B. Accidental Laboratory Infection with Human Dengue Virus. *Proc. Soc. Exper Biol & Med* 1943 May 68 No. 1 198-200 1 fig

In the course of the experiments described in the previous paper one of the assistants accidentally received a drop of dengue-infected serum in his eye. Seven days later a macular rash was seen on the face and after a further period of two days there was a sudden attack of fever and vomiting. The temperature remained between 101° and 103°F for about six days.

The mouse-neutralization test was negative on the first day of the fever and became progressively more strongly positive in tests made on the 13th, 25th and 45th days after the onset.

John B. D. Macfar

## PLAGUE

PUBLIC HEALTH REP. Wash. 1943, Aug 20 v. 63, No. 34 1102-3. Plague Infection reported in the United States in 1947

No naturally acquired human case of plague has been reported in the United States since 1943. A fatal case is now reported in a 12 year old boy living in Alturas, Modoc County, California. It is believed that he was infected near a Ranger Station, 13 miles south-east of Alturas. Wood rats in this area were found to be infected later in the year. Plague infection had previously been reported from Modoc County in 1934, 1935, 1936 and 1942.

It is significant that the last two human cases of plague reported from the U.S. in 1943 and 1942 respectively occurred in Siskiyou County which borders Modoc County to the west.

Gradual extension to the east of infection in wild rodents or their ectoparasites has already been noted (*this Bulletin* 1948, 43:171). This fact coupled with the occurrence of occasional human plague infections in the U.S. indicates that the disease is still a problem in that country and that unless control is maintained rigorously, plague infection can be expected to extend into any city in the western States having a substantial rat population and might well even spread to rodents of the Great Plains, the Mississippi Valley and the eastern States.

During 1947 infection was reported in 13 species of wild rodents or their parasites in six western States, namely Arizona, California, Colorado, Hawaii,



Washington and Texas The pools of ectoparasites in which infection was found by mass inoculation were principally fleas, but infection was found in a pool of lice in one case and a number of pools of fleas also included ticks and lice

A lengthy table sets out in detail the number of pools of ectoparasites and of rodents found to be infected in the counties of the six States concerned on various dates during the year [Infections reported in 1946 are discussed in the abstract quoted above]

H J O'D Burke-Gaffney

## AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

NEAL, R A *Entamoeba histolytica* in Wild Rats caught in London  
J Hygiene 1948, Mar, v 46, No 1, 90-93, 1 text fig & 2 figs on 1 pl  
[11 refs]

Natural infections of rats with *Entamoeba histolytica* have been reported on several occasions from different parts of the world, but this is the first record of its occurrence in rats of England These spontaneous infections are of some epidemiological importance, since it is conceivable that wild rats might act as reservoir hosts of human amoebiasis The author describes the finding of an amoebic infection in seven out of eleven wild rats caught in a London house, among the inhabitants of which were two Cypriots passing abundant cysts of *E histolytica* in their stools It was also shown that the trap between the sewers and the drainage system of the house in question was absent, thus enabling the rats to gain access to the house From these facts it would seem that the infection was acquired by the rats from cysts of a human strain of *E histolytica* The active forms of the amoeba were identical with *E histolytica*, cysts were scanty and represented by immature forms, but in culture typical quadrinucleate cysts developed Infection in the wild rats was restricted to the caecum, in which no lesions were detected However, when cultures of amoebae isolated from wild rats were inoculated intracaecally into newly-weaned white rats they invaded the caecal wall, producing ulceration The amoebae ingested tissue fragments, bacteria and red blood corpuscles The infection in the experimental animals was successfully treated with emetine hydrochloride administered at a dilution of 0.002 per cent in the diet

The paper is illustrated by figures of the trophic amoebae and their cysts, and by photomicrographs of sections of the caecal lesions

C A Hoare

MILLER, M J & CHOQUETTE, L P E Studies on Amoebiasis in Canada.  
Part I The Incidence of Intestinal Protozoal Infections in Two Institutionalized Groups in Canada Canadian J Res Sect E Med Sci  
1947, Feb, v 25, No 1, 1-4

In a previous survey of 47 orphanage children in Saskatchewan, the senior author [this Bulletin, 1940, v 37, 113] found *Entamoeba histolytica* in the stools of 23 per cent on a single examination, despite a low local clinical incidence of the disease

In order to pursue this subject in Canada, the present authors studied subjects from two institutions in Montreal, namely (1) an orphanage of 163 boys, aged 8 to 10 and (2) an Old Men's Home, with 151 persons aged 32 to 95 (average 59 to 70 years) Orthodox methods of examinations were employed

In group (1) 153 or 97 per cent of the boys and in group (2) 107 or 71 per cent of the men harboured one or more species of intestinal protozoa. The detailed percentage results were as follows:—

	Boys	Men
<i>E. histolytica</i>	37.0	21.5
<i>E. al</i>	27.0	37.0
<i>E. magna</i>	60.5	52.0
<i>I. butschli</i>	3.5	5
<i>G. lamblia</i>	49.0	6.0
<i>C. mesnili</i>	7.0	0

The cysts of *E. histolytica* found were classified into the large and small races as defined by SARANTO *et al.* [this Bulletin 1943 p. 40-53] with the following percentages of each:—

	Boys	Men
Large race	28.5	8.5
Small race	17.5	13.0
Large and small race	5.5	1.0

Despite the limited numbers in the groups examined, the results tend to confirm the previous Saskatchewan findings that intestinal protozoa are common in persons in institutions in Canada. The authors state that the results "add further support to the frequently demonstrated but still largely unrecognized fact that the intensity of *E. histolytica* infections is mainly dependent on the sanitary standards of a people and not related to their geographic locale.

The groups were comparable except in age but the extremes of age tended to make their sanitary levels similar. Almost all the subjects had been born in Quebec.

It will be noted that the incidence, intensity and multiplicity of all the parasites was greatest in the boys. A further point of interest is that *Candida* was common in the boys and rare in the older men and while *E. al* was commoner than *E. magna* in the former the reverse was true in the latter.

The incidence of the small race of *E. histolytica* was high indeed in the older group, it was commoner than that of the large race. The authors discuss this incidence and suggest that although the small race is generally assumed to be a relatively minor role as a cause of amoebiasis, its pathogenic status requires to be determined definitely by further studies, both because of its relative frequency and because of the difficulty of distinguishing it from *Endolimax nana* in fresh smears. [See also this Bulletin 1947 v. 44 pp. 1-4 of 1948 v. 45, 517.]

H. J. O. D. BURKE-GALLAGHER

GROOM, D. H. Appendicitis due to Entamoeba histolytica. India Med. Gaz. 1948, Apr. v. 83, No. 4 185-6

TERRY, L. L. & BONIFACE, J. The Importance of the Complement Fixation Test in Amoebic Hepatitis and Liver Abscess. Southern Med. J. 1948 Aug. v. 41 No. 8 681-70, 81, 101-5.

ly diagnosis of amoebic hepatitis or of amoebic liver abscess difficult. presence is suspected. By the time gross physical signs such as deformity develop are well advanced and the

damage extensive From collected reports, OCHSNER and DEBAKEY [this *Bulletin*, 1943, v 40, 915] recorded that in only 474 (11.6 per cent) of 4,091 cases of amoebic liver infection has the presence of a gut infection with *Entamoeba histolytica* been proven. A satisfactory complement-deviation test would therefore be of great value in questionable cases of amoebiasis, especially in those with liver involvement. The difficulty in this test lies in the lack of a potent antigen.

For some years, a group in the Division of Tropical Diseases of the National Institute of Health, U.S.A., has been examining the complement-deviation test for amoebiasis. In conjunction with this study, the Medical Service of the U.S. Marine Hospital, Baltimore, has made clinical applications of the test. The present paper is concerned with these.

Fifteen cases of amoebic hepatitis or liver abscess were thoroughly investigated between 1943 and 1947. The patients were males, aged between 17 and 64 years, of various races and nationalities. According to KLATSKIN's classification [*Ann Intern Med*, 1946, v 25, 601] there were 6 patients with acute and 2 with chronic hepatitis, and 5 with acute and 2 with chronic abscesses. A complement-deviation test was performed on each of these by staff at the N.I.H., who were unaware of the clinical diagnosis. The antigen used was obtained by placing an inoculum of amoebae in a dialysing tube in a coagulated egg-white medium covered with Locke's solution fortified with vitamins. After incubation at 37°C for 144 hours, the contents of the tubes were pooled, merthiolate, 1/1,000, was added, and the mixture was refrigerated at 50°C for 3 days. It was then centrifuged for 15 minutes at 20,000 r.p.m., the supernatant fluid was removed and dialysed in tap water, and then in 3 changes of distilled water. The contents of the dialysing tube were evaporated before a fan to about one-fifth their volume before dialysis, the concentrate was again centrifuged at 20,000 for 15 minutes, and the residue was discarded. The supernatant fluid was again merthiolated after being made isotonic with sodium chloride.

Stool examinations were done on 14 of the 15 cases, and of the 14 only 3 were found to contain *E. histolytica* before treatment. Three more were subsequently found to harbour parasites in the gut. In the case of 2 patients the complement-deviation test was not done until some time after specific treatment had been given, one of these gave a positive test, the other a negative. In the remaining 13 cases the test was performed before treatment, 10 gave consistently positive reactions, 2 gave initially negative (false negative) reactions, but on repetition within a few days the test had become positive, one gave a negative reaction on the only occasion the test was done prior to treatment. It was found that the antigen used in each of these 3 cases where negative readings were obtained was lacking in antigenic potency. All 3 cases at subsequent dates gave positive reactions, although re-examination of the same serum of one of them with a potent antigen continued to give a negative result. There was no record in the hospital of a false positive test. [No mention is made of the number of controls examined.] It has not been determined how long after successful treatment of an amoebic liver abscess a positive complement-deviation test persists. In some cases there is a reversal within 1 to 3 weeks, in one case the test remained positive for 2 years, and the patient was clinically well for a period of at least 3 years.

[In the reviewer's opinion the percentage of proven intestinal infections with *Entamoeba histolytica* in the cases referred to in this paper, and in the literature cited indicates a lack of experience and skill in their detection. As the authors indicate "there has been disagreement among experts as to identification of amoeba even when examining the same slide," an observation which reinforces the above comment.]

A R D Adams

D2

DRAME E. H. & WARTHIN T. L. Amiable Abscess of the Liver. Therapeutic Problems in various Types of Late Hepatic Amoebiasis. *New England J. Med.* 1948 July 8, v. 239 No. 4, 45-9

Six cases of late amoebiasis of the liver are described. None had previously been diagnosed as being infected with *E. histolytica*. The onset was usually acute with signs referable to the liver.

The clinical material is divided into three groups—simple amoebic hepatitis, a large liver abscess remaining localized, and a large abscess which had penetrated through the diaphragm. Only one was classified as diffuse hepatitis and was treated by chemotherapy alone.

Two had abscesses of significant size that had not drained into the pleural or peritoneal cavities. These were treated by chemotherapy and aspiration. After the institution of emetine therapy an incision was made in the abdominal wall to permit, under direct vision, the introduction into the abscess of a large aspirating needle. This aspiration was followed by the instillation of penicillin into the abscess cavity and closure of the abdominal wall without drainage. The two abscesses which had penetrated through the diaphragm were secondarily infected and these were treated by open drainage. In the sixth case the abscess had drained spontaneously into the right pleural cavity and through the bronchial tree. The patient was treated by chemotherapy and aspiration of the empyema fluid by thoracentesis.

All were treated by intramuscular emetine in a single dose of 1 grain daily for eight days and by two subsequent courses, each of six days duration. At the termination of each emetine course iodoform was given by the mouth, commencing with 4 grains three times daily increasing to 15 grains three times daily for 10 days. Penicillin was injected intramuscularly in doses from 30,000 to 50,000 units every three hours.

Some evidence was obtained by studies *in vitro* in the fifth case that development of resistance to emetine may take place. Amoebae from this patient grew in concentrations of emetine which were much higher than the control strains tested, indicating drug resistance.

Iodoform was found to be satisfactory for eradication of *E. histolytica* cysts.

The onset of symptoms referable to the abscess were often acute and without premonitory symptoms. In the second case the physical signs suggested acute cholecystitis. The white-cell count varied from normal to marked elevation. Examination of the faeces was positive in three out of the six. After spontaneous drainage by hepatobronchial fistula the sputum was found to contain trophozoites of *E. histolytica* in two cases, while the exudate from abscess cavities with inadequate drainage contained large numbers of motile trophozoites.

P. M. LOW-BALLO

CROSNIER, R. MARLE, BARNIER, MOUINIER & TABI. Le Traitement de la dysenterie amibienne par les extraits d'*Heliconia* surinamensis.  
[Treatment of Amoebic Dysentery with Extracts of *Heliconia*.] *Bull. Acad. Nat. Med.* 1948, v. 132, No. 19-20, 336-8.

The alcohol of *Heliconia* *surinamensis* acts specifically on the dysenteric amoebae and cysts. To thirteen patients with acute amoebic dysentery was given the total alcohol of the plant. From 9 the amoebae disappeared in 4 cases there was improvement. Similar results in 16 patients with cysts in the stools led to the disappearance of the cysts.

Thirteen other patients with acute amoebic dysentery were treated with cocaine hydrochloride. One of these did not complete the course. Eight

intolerance of the drug, the remainder were cured by the treatment. Conessine hydrobromide appeared to be as efficient, and to be free from toxicity

A R D Adams

PIEKARSKI, G. Zur Frage der Cystenbildung bei *Dientamoeba fragilis* [Encystation in *Dientamoeba fragilis*] *Ztschr f Hyg u Infektionskr* 1948, Apr 1, v 127, Nos 6/8, 496-500, 7 figs

The author has re-discovered, in the stools of an inmate of an institution, cyst-like structures corresponding to the so-called "Bosman-cysts" previously described by BRUG [this *Bulletin*, 1937, v 34, 514]. While Brug left the question regarding the identity of these bodies open, the present author regards them as cysts of *Dientamoeba fragilis*. Subsequent examinations of stools of 133 other persons revealed in eleven cases the presence of the same structures in association with the amoeboid forms of *Dientamoeba*, while in 32 cases only the amoebae and in 21 only the "cysts" were found.

The cysts are rounded or ovoid, measuring  $4-9\mu \times 4-6\mu$ . When stained with iron haematoxylin a distinct cyst-wall is seen around the enclosed body, which is detached from the wall and contains two dark-staining granular structures. Though these do not always show the characteristic structure of the nuclei of *Dientamoeba*, their nuclear nature was revealed by Feulgen's reaction. In addition there were a number of "chromidial bodies" [=chromatoids]. The author claims to have seen all transitions from the "vegetative cells" of *Dientamoeba fragilis* to these cyst-like bodies, which left no doubt in his mind that they belonged to the same parasite. The appearance of these cysts is shown in a series of figures. He was unable to undertake any further investigations—by experimental infections and cultivation—on the nature of these cysts.

C A Hoare

COSTA, R. S. *Dientamoeba fragilis*. Jepps y Dobell, 1918. Primeros casos señalados en nuestro país. Consideraciones epidemiológicas [*Dientamoeba fragilis*. The First Cases recorded in Cuba]. *Rev Kuba Med Trop y Parasit* 1948, June, v 4, No 6, 115-18 [24 refs.]

In 1941 the author heard of certain skin diseases associated with, and thought to be due to, intestinal parasites. He, therefore, has looked for these in patients coming for treatment of exudative or desquamating eczema, prurigo, urticaria and other skin affections allergic in nature. Eighty-two patients with these dermatoses have been examined and 52 of them had intestinal protozoal parasites. Among 76 patients whose faeces contained protozoa, 4 of the author's patients and one sent in by another practitioner were passing *Dientamoeba fragilis*. The fifth was a child of 7 years, with entero-colitis whose faeces contained also *Entamoeba coli* and *Giardia intestinalis*. Case 1 was in a man of 41, with eczema of hands, face and neck which had troubled him for about 20 years, he had *D. fragilis*, *E. coli*, *Endohmax nana* and *Chilomastix mesnili*. He was given Enterovioform, 3 tablets daily, to a total of 40 tablets. The symptoms cleared up, but a couple of months later they returned and *D. fragilis* was again found. Case 2 was a man of 27, with generalized eczema and prurigo for  $2\frac{1}{2}$  years and had *D. fragilis* in his stools. He, too, was given Enterovioform, improvement was rapid and the cutaneous lesions disappeared. He was not seen again. Case 3, a man of 53 years, with pruritus ani for 5 years, *D. fragilis* was abundant. He was given Carbantren and slight improvement took place. Case 4, a man of 18, with generalized scaly eczema, especially on face and hands, 7 years duration. *D. fragilis* very numerous. He was treated with Carbantren, 3 tablets daily for 10 days, repeated after an interval of 8 days. The skin condition was cured and there had been no return when he was seen again nearly four months later.

H Harold Scott

FILHO F. S. & CASTRO E. L. Patogenia e quadro clinico da giardíase [Pathogeny and Clinical Picture of Giardiasis.] *Rev. Brasileira M. I.* Rio de Janeiro. 1948, Jan., v 3 No. 1 1-15. [Bibliography] English summary.

After noting the opinions of many authors regarding the question of the pathogenicity or mere simultaneous presence of *G. intestinalis* & whether symptoms accompanying the presence of the protozoan are aetiological or connected, the authors record the facts in 15 patients under their observation. The chief subjective complaints were of epigastric pain, nausea, especially in the morning, pyrosis, dyspepsia, bitter taste in the mouth, diarrhoea alternating with constipation, flatulence and headache—symptoms somewhat vague and indeterminate. They believe that the presence of the parasite in the gall-bladder or bile causes spasm of the sphincter and stasis of the bile and some degree of inflammation of the bladder wall. They conclude therefore that *G. intestinalis* has a definite pathogenic action even though a mild one. Treatment by atabrin 0.1 gm. thrice daily for 5 days, proved quite satisfactory.

H. Harold Scott

HERRLICH A. & LIEBMAN H. Die menschliche Coccidiose. (Weitester Beitrag zur Kenntnis der menschlichen Coccidien.) [Human Coccidiosis. (Further Contribution to the Knowledge of Human Coccidia).] *Ztschr. f. Hyg. u. i. f. Infektionskr.* 1944 Nov 12, v 128 No. 1/2, 23-36 6 figs.

This is a continuation of the authors' previous work on human coccidiosis [this *Bullet.* 1944 v 41 782]. In the present paper they report the results of an experimental study, the main objects of which were to determine the clinical manifestations of the infection and the host-specificity of *Isospora belli*.

An exceptionally heavy infection in a patient (about 10 oocysts per microscopic field in faecal smears) enabled them to carry out experimental infections in man and lower animals. The oocysts were allowed to mature in an incubator at 37°C., after which (30 hours later) they were diluted in water and introduced into the stomach of volunteers by means of a catheter, each receiving about 20 cc. of the suspension containing about 100,000 oocysts. The total number of volunteers was ten, 5 of whom were inoculated with the suspension, 2 with centrifuged oocysts and 1 with immature oocysts while the others, serving as controls, received 20 cc. of the filtrate from the infective material. The persons to whom ripe oocysts were given started passing immature oocysts in the stools between the 9th and 16th days after infection, their discharge ending after 21 days but those who received centrifuged or immature oocysts failed to acquire an infection. It was thus confirmed that *I. belli* undergoes a definite cycle of development in the human intestine. The infection was produced in the stools. Human coccidiosis is therefore a self-limited disease. Attempts to infect young kittens, pups, mice, guinea-pigs and rabbits were unsuccessful. It is concluded that *I. belli* cannot be regarded as a variant of the common group of *Isospora* of cats and dogs but is a parasite specific to man, though the existence of some unknown animal reservoir cannot be excluded.

C. A. H. Scott

See also p 1119 CASAS SACRE Impresiones parasitológicas a través del Seguro Social Mexicano.

CRAND, Charles Franklin. Laboratory Diagnosis of Protozoan Diseases.

This book is reviewed on p. 1133.

## YAWS

APTED, I, HARDING, R D & GOSDEN, M A Clinical and Serological Follow-up of Yaws Cases treated by Acetylarsan and Bismuth Sodium Potassium Tartrate *Trans Roy Soc Trop Med & Hyg* 1948, July, v 42, No 1, 55-64

This paper reports observations in eastern Sierra Leone on the cure rates following administration of acetylarsan and bismuth sodium potassium tartrate (BSPT) alone and in combination in two areas about 70 miles apart

In the first area observations were made at the same intervals after treatment with one or both of the drugs, in those patients who showed the worst yaws lesions in a community which had enjoyed facilities for treatment for some years Kahn and modified Ide tests were used, but the latter were found unsatisfactory in following the results of treatment The patients treated were suffering from secondary yaws, predominantly non-infectious plantar lesions

After 6 doses of acetylarsan 4 cc [0.94 gm diethylamine acetarsol], 61 per cent of cases had no lesions and the serum from 50 per cent gave weak (15) doubtful (15) or negative (21) Kahn reactions After 3 doses of acetylarsan 3 cc and 4 doses of BSPT 3 grains [0.18 gm] 49 per cent had no lesions and only 21 per cent had weak (4), doubtful (11) or negative (7) Kahn reactions After 6 doses of BSPT 4 grains [0.25 gm] no lesions were found in 32 per cent and 9 per cent had infectious relapses and the Kahn results were weak (2), doubtful (4) or negative (7) in only 13 per cent All observations were made 6-7 months after treatment, injections were given at intervals of one week and the numbers of patients in individual groups ranged from 28 to 120 Sera from 37 of these cases were examined 12 months after treatment, when only 2 were weak or doubtful and 5 negative, the rest were positive Six months previously the same patients had shown 11 weak and 5 negative Thus it was seen that although acetylarsan was moderately effective, the particular BSPT preparation used was of limited value either alone or with acetylarsan The marked seasonal variations in incidence of yaws lesions complicated the full assessment of therapeutic effect

In the second area observations were made at varying intervals after standard courses of acetylarsan and BSPT together All patients with definite signs of yaws were treated from a community where previously treatment was not so readily available Tertiary yaws cases were omitted from this study Clinical examinations were made at intervals of 6, 12 and 24 months and Kahn tests were carried out at 6, 18 and 30 months The doses of acetylarsan were reduced from 5 cc [1.18 gm diethylamine acetarsol] to 4 cc [0.94 gm] and later 3 cc [0.71 gm] because of toxic reactions, and the dosage of BSPT was 3 or 4 grains [0.18 or 0.25 gm] Both drugs were given on the same day, intramuscularly, and repeated at intervals of 5 days, usually 4 pairs of injections were given

The passage of time made little difference in the clinical or serological findings Of patients with infectious yaws 70, 64 and 76 per cent had no lesions after 6, 12 and 24 months, and 52, 58 and 71 per cent had weak, doubtful or negative Kahn reactions after 6, 18 and 30 months Of patients with non-infectious yaws, 58, 34 and 45 per cent had no lesions and 69, 72 and 69 per cent had weak or negative Kahn tests after the same time intervals The numbers in the groups ranged from 27 to 154, larger doses of drugs had been received by patients followed for the longer times

The authors stress the importance of frequently repeated observation in assessing the clinical relapse rate They conclude that acetylarsan in the doses used will banish the more marked signs of yaws for at least 2½ years and will

perhaps permanently cure one-third of cases (secondary) and that it will render most of the remainder quiescent for an indefinite though prolonged period. In later work they have replaced BSPT by bismuth salicylate in oil, with striking improvement in immediate results. Further data on this are to be published later.

(This paper is the result of much field work and analysis. The reviewer feels that fuller knowledge of secondary and tertiary plantar and palmar jaw lesions, at present non-existent will remove the necessity of using such unsatisfactory terms as "active", "inactive", "infectious" and "non-infectious", each of which comprised a group. Lesions with no certainty that the "inactive" and "non-infectious" groups do not include both secondary and tertiary lesions. Since the publication of this paper HARDING has found that the bismuth content of the BSPT used was only about 4.5 per cent. while that of bismuth salicylate (B.P.) is about 60 per cent.)

C. J. Hackett

## LEPROSY

VIRIMA BRAGA, R. Contribuição ao estudo da lepra no meio industrial do Distrito Federal. [Leprosy in Industry in the Federal District (Brazil).] *Rev. Brasileira Med.* Rio de Janeiro, 1948 Apr. v. 5 No. 4 259-60 6 graphs.

During the nine-year period, 1 August 1938-31 July 1947 among 68, 64 patients examined at the Industrial Institut 3,008 were suffering from skin diseases and 231 from leprosy, i.e. 7 per cent. of the total examined were skin affections and 0.35 per cent. were leprosy. The numbers varied considerably from year to year: 20 only in 1941, 39 (a peak number) in 1944. Of the total, 483 were suffering with the mixed type, 93 with the neural and 40 with the lepromatous type. By far the greater proportion were males, but this has little significance as male employees far exceed the females. The majority were between 20 and 40 years of age and the figure was higher in the third decade than in the fourth. As regards trades most of the cases were among tailors, bakers and seamstresses [infection from clothes?]. Those engaged in these occupations should be repeatedly and periodically examined.

H. Harold Scott

VALLE, S. Diagnóstico precoce da lepra. Parte I, II & III. [Early Diagnosis of Leprosy.] *Rev. Brasileira Med.* Rio de Janeiro, 1948 Apr., May & June v. 5, Nos. 4, 5 & 6, 2nd-95 377-87 444-54 39 figs. (11 coloured) [Bibliography].

This article contains a good general account of leprosy in its various aspects. It is not easy to see, however, why the title is "early diagnosis" for later stages of the disease are included, short of actual mutilation. The following indications of the disease are each discussed in turn: the anaesthesia and its usual distribution, the neuritis and neuralgia, the wasting of muscles, particularly those served by the median, the external popliteal, the facial and the supraorbital nerves. The ocular lesions are fully described, with excellent reproductions in colour next the affection of the nasal mucosa and clinical tests, the histamine and pilocarpine tests and the diagnostic differences between lepra and syringomyelia, examination for the bacteria, the Mitsuda reaction, the chief features of the lepromatous, the tuberculoid and the non-characteristic form and



ending with remarks on other forms of localized anaesthesia, maculae, and nodule formations, carcinoma, sarcoma, sarcoid, yaws and others

H Harold Scott

DA VEIGA, S As lesões osteo-articulares da lepra através das imagens radiográficas [Bone and Joint Lesions in Leprosy, with Radiographic Illustrations] *An Inst Med Trop* Lisbon 1947, Dec, v 4, 149-60, 24 figs on 12 pls English summary

The author took 400 radiograms of the hands and feet of 100 leprosy patients in the Central Leprosarium of Goa Fifty-eight were males, 42 were females, between the ages of 12 and 67 years, the numbers in successive decades being 5, 17, 27, 28, 17 and 6 The duration of the disease ranged up to 5 years in 23 patients, 6-10 years in 37, 11-15 years in 13, 16-20 years in 10, 21-28 years in 9 in the remaining 8 the duration was not known

The author divides his patients into 5 groups (i) Those with cutaneous lesions only (7 in number), (ii) with marked cutaneous and slight nerve manifestations (18), (iii) purely nerve cases (42), (iv) with marked nerve and slight skin affection (11), (v) with nerve and cutaneous lesions about equal (22) The diagnosis had to be made between leprosy on the one hand and, on the other, tuberculous or syphilitic osteitis, sclerodactylia, scleroderma, Besnier-Boeck disease, syringomyelia and tabes

The pathological process was chiefly destructive, rarefying osteitis and osteoporosis, with cyst-like formation and more extensive destruction resulting in mutilation Some of these, in particular the osteoporotic changes, would seem to be due primarily to vascular disturbance, whereas those changes involving the joints as well as the bones result from leprotic nerve involvement Hence the osteo-articular lesions are most common in those with the nervous form of the disease and were more marked in the feet than in the hands [The article is illustrated with 24 excellent radiographic reproductions and more can be learnt from a study of these than from any abstract or even pages of letterpress]

H Harold Scott

MONTEL M L R Deux cas de réactions lépreuses aiguës, fébriles traités respectivement par le bleu de méthylène et l'émétique [Two Cases of Acute Febrile Leprosy Reaction treated respectively with Methylene Blue and Tartar Emetic] *Bull Soc Path Exot* 1948 v 41 Nos 5/6, 312-18 2 charts

FONTL, J & ROSSELL C S C Contribuição ao tratamento da lepra pelo 'promin' Controle dos doentes pela pesquisa do bacilo no sangue [Treatment of Leprosy by Promin Control of Cases by Examination for Bacillaemia] *Brasil-Médico* 1948, Apr 17 & 24, v 62, Nos 16-17, 170-76

The authors treated 8 cases of the lepromatous type of leprosy with Promin All had bacilli in the nasal mucus, in specimens from the skin scarifications and in samples of blood Three methods of blood examination were used, that of Crow, of Rivas and of Gomes de Faria, all cases were positive with the last but not all with the other two Of the 8 patients 7 were males, 1 was a female, their ages ranged from 19 to 45 years and the number of injections given was up to 240, in series of 10-18 injections, the average dose about 4 gm (3.8-4.4) Slight exacerbation of symptoms succeeded the beginning of treatment—focal reactions or nodular erythema—but this disappeared with further treatment The nodules softened, nasal obstruction and coryza disappeared, the erythematous patches were clearing and weight increased Nervous symptoms

remained unchanged. In other respects there was no change: bacteria were still present in the nasal mucus, the skin, the blood, and the Mitsuda reaction (negative in all but one) remained the same. The bacteria, however, though present, were more fragmented and less acid fast. Details are given of each of the eight treated.

H. Harold Scott

PICCARDI G. & RADAZZI G. Sulla ricerca sul comportamento dei composti di Molibdeno negli organi leprosi. [On the Behaviour of Molybdenum Compounds in Leprous Tissues.] *Spectrochimica Acta* 1948, v. 3, No. 2, 233-4 (16).

That methylene blue injected into the living body stains the tissues and organs attacked by *Mycob. leprae* and electively the bacteria themselves is well known. It is also known that ammonium molybdate and methylene blue in solution when added together produce a dark blue solid. Hence there arose the idea of localizing, as it were, the molybdate in the affected tissues by means

of the methylene blue and obtaining thereby a more energetic action of the drug. The following researches were carried out: (1) A leprous nodule stained with methylene blue in a young patient, was extirpated and divided into two. One part was immersed for a certain time (not stated) in a solution of Am. molybdate, the other not. When subsequently immersed in 95 per cent. alcohol the latter was rapidly decolourized, the former retained the colour, confirming the fixing action of the molybdenum. (2) The patient who had many lepromata, some of which were stained with methylene blue was given a series of intravenous injections of 1 per cent. Am. molybdate. Five days after the course ended, two nodules were extirpated, one which had been stained, and one which had not and was of the normal red colour. The nodules after treatment with fuming nitric acid gave place to an oily residue. Examined petrioscopically in the UV area, the lines of molybdenum were plain in both the nodules and to about the same degree in both. (3) In order to demonstrate the fixation of molybdenum in the nodule stained with the methylene blue 3 months after the course of treatment two more nodules, one blue and one unstained, were injected from the same patient and the same procedure carried out. No traces of molybdenum could be found on spectroscopic examination. It had been completely eliminated, indicating that the methylene blue had not the effect of fixing the molybdenum.

H. Harold Scott

DE SOUZA-VASCONcelos Heracles-César. História da Lepre no Brasil. Vol. II.

This book is reviewed on p. 1132.

HERNANDEZ LUIS. Índices Bibliográficos da lepra 1900-1945. Vols. I, II & III.

This book is reviewed on p. 1133.

## HELMINTHOLOGISTS

DE MEIRA M. T. V. & AGUIAR J. F. P. & SIMÕES T. S. Contribuição para o estudo do parasitismo intestinal na Ilha do Sal, Boa Vista e S. Nicolau (Cabo Verde). Intestinal Parasitism in the Islands of Sal, Boa Vista, and S. Nicolau (Cape Verde). *J. J. Med. Trop. Lisbon* 1947 Dec. v. 4, 239-54. English summary (10 lines).

This study of more than local interest bears witness to inter-communication between the islands of the archipelago, and the hope to be an accurate statement established

on the island of Sal] There is no statement of the population of these islands and the numbers examined—by the Willis technique—were small, and this fact should be borne in mind in interpreting the findings

In S Nicolau, 117 individuals were examined from 24 localities [in 9 of these only one was examined] and 92 (78.6 per cent) were passing hookworm ova, and 87 of these other ova also, 44 of them *Ascaris* and *Trichuris*. Blood examination revealed but little anaemia, whether the patients had hookworm alone, or with other helminths, or the latter without hookworms. The average number of red cells was  $3\frac{1}{2}$  to  $3\frac{1}{2}$  million per cmm (in those without parasites 3,630,000), haemoglobin about 50 per cent (in the non-parasitized 67.7 per cent), eosinophiles ranged up to 29 per cent, with an average of 8.2 in those with ankylostomes only, 11.4 in those with other helminthic infestations also, an average of 9 in those with helminths other than ankylostome. Those without any intestinal parasites had an eosinophilia of 7–11 per cent. average 10 [no reason is offered in explanation of this]. Of 125 who had never left the island 94 were infested (75.2 per cent) most (59) with *Ascaris*, next (17), with *Trichuris*.

Specimens of blood were examined also for filariasis, 100 were taken in the daytime and 84 between 9 p.m. and midnight. Embryos of *Acanthocheilonema perstans* were seen in 5 of each (day or night specimens) and in four cases in both.

In the island of Sal 278 individuals were examined for intestinal infestations and 83 (30 per cent) were positive. 19 showed *Ascaris* ova, 10 *Trichuris*, there was none with hookworms. 36 showed *Entamoeba histolytica* and 15 *Giardia intestinalis*.

In Boa Vista, only 85 were examined, 28 were positive, 10 with *Ascaris*, 11 with *E. histolytica*, 7 with *G. intestinalis*, again here ankylostomes were not found. H Harold Scott

See also p 1120, TALIAFERRO, The Inhibition of Reproduction of Parasites by Immune Factors

See also p 1119, CASIS SACRF, Impresiones parasitologicas a traves del Seguro Social Mexicano

TALAAAT, S M Renal Concentration Test in Urinary Schistosomiasis and the Effect of Tartar-Emetic on It J Roy Egyptian Med Ass 1948, June, v 31, No 6 481-6

The ability to concentrate the urine is usually the first function to fail in renal disease. The "posterior pituitary test" for this consists of the administration of 10 units of posterior pituitary extract subcutaneously, after the patient has emptied his bladder and a record of the blood pressure at 5, 10, 15 and 30 minutes, and of the specific gravity of the urine at hourly intervals for 3 hours, after the injection 1,020 being taken as normal.

Of 15 apparently normal individuals only one failed to concentrate urine to an S.G. of 1020. Of 24 cases of pure urinary schistosomiasis (i.e. abnormality confined to the urinary tract), examined both before and after treatment with tartar emetic, 4 failed to concentrate the urine adequately. Tartar emetic treatment it is considered, did not impair the kidney concentration power, indeed in one case the power of concentration after treatment was found adequate where previously it had been deficient. Kidney function is impaired in urinary schistosomiasis, the incidence being thrice that found in controls by the posterior pituitary test [The data supplied in the text and the tables are unconvincing]. A R D Adams

BLAIR D. M. & ROSS W. F. Observations on the Use of Cercarial Antigen in the Diagnosis of Schistosomiasis. *Ann. Trop. Med. & Parasit.* 1948 Apr. v. 4<sup>th</sup> No. 1 48-51 1 graph.

The authors describe two methods of making antigens from cercariae for the diagnosis of schistosomiasis. OLIVER GONZÁLEZ and PRATT (this *Bulletin* 1948 v. 43 343) and HATZIN and MOST (ibid. 1947 44 440) made an antigen from cercariae shed by snails infected with *Schistosoma mansoni*. The cercariae were stored as a dried powder after having been centrifuged down. The liquid antigen was made from this powder by a 1:5000 dilution with 0.5 per cent. carbol-saline. ALVÁS and BLAIR (this *Bulletin* 1948, v. 43, 344 1947 v. 44 828 827) made another antigen from mammalian cercariae presumed to be those of *S. haematobium* shed by naturally infected *Physopus f. v. a.* Water from a pond in which the snails were kept was poured through filter paper to trap the cercariae, a rough estimate of the number of cercariae (usually 1,000 to 15,000) trapped on each filter paper being made. The antigen was stored on these filter papers. Liquid antigen was made by macerating the filter paper in 1 per cent. carbol-saline for 48 hours. 1 cc. of carbol-saline being allowed per 2,000 cercariae the fluid being finally expressed and diluted with an equal part of normal saline. The final concentration of antigen works out at the products of 1,000 cercariae per cc. The dose given for each skin test is "about 0.03 c.c.m. which equals the products of 33 cercariae."

CANNON has objected that when "wild" snails are used the exact species of the cercariae is not known. The present authors do not claim that all the cercariae used were those of *S. haematobium* and maintain that no claim has ever been made that antigens made from cercariae are species specific. Oliver González and Pratt (loc. cit.) used antigen from *S. mansoni* against diagnosis infection with *S. japonica*. They recommended that the initial weal produced should have a diameter of 4 mm. and consider as positive a weal the diameter of which has doubled to over 8 mm.

Discussing this question, the present authors give a table showing the diameters of weals shown by 39 positive reactors and 38 negative patients at intervals of 5 minutes up to 25 minutes after the injections. The positive group consisted of 1 European, 17 European children and 21 African school children. 22 of these were infected with *S. haematobium* 3 with *S. mansoni* 6 with both these species and 8 were passing no eggs. The negative group consisted of 7 Europeans, 1 adult African and 33 African school children. In each of the subjects a control weal was produced with carbol-saline.

The table shows that the antigen weals increased in size in all the positive reactors in comparison with the control weals up to a maximum reached in 15 to 20 minutes after the injections. In the negative group the antigen and control weals showed little or no increase in size. The authors emphasize that the optimum time for measuring the weals is 15 minutes after the injection. Only a few of their subjects showed doubtful reactions. Weals whose diameters increased only to one and three quarters or twice the size of the initial weal. The authors used conetell paper discs with diameter of 8 mm. as aids to measurement and a series of cine photograph of the development of the weals of one subject was projected on to squared paper so that the sizes of the weal could be measured and expressed in the graph reproduced in their paper.

Comparison of weals produced by stocks of 5 old antigen 1 of which the 2 oldest were made in 1933 and 1945 the other being about a year old, showed no significant difference in the reactions produced by these different antigens. The authors advocate the use of control injection for individual diagnosis, especially in Europeans, but they consider that controls are not necessary when

Africans are being tested in mass, because skin allergy is believed to be rare in African subjects, if it occurs at all  
G Lapage

MARTINEZ-VILLAFANE, H & LANG, A A The Treatment of Schistosomiasis  
Mansoni with Neostibosan Preliminary Report Bol Asoc Med de  
Puerto Rico 1948, June, v 40, No 6, 128-30

The authors treated 25 adult males suffering from *Schistosoma mansoni* infections with Neostibosan The drug was given intravenously daily for three days (50, 100 and 200 mgm respectively) and then in doses of 300 mgm on alternate days to a total of 8.45 gm In only one case was the treatment discontinued because of untoward reaction (a total of 4.25 gm had been given) Reactions in two other cases were controlled by the antihistaminic drug Pyribenzamine

Immediately after treatment, 7 patients showed "live" ova either in stools or rectal biopsy, 10 showed dead eggs in the biopsy, but none in the stools and 8 had no ova showing in either

In follow-up studies of 13 cases from one to seven months after treatment, 9 showed positive stools within five months but the follow-up is not yet complete The author believes that the number of failures will be found to be higher and concludes that Neostibosan has not sufficient parasitotropic effects to warrant its use in the treatment of *S. mansoni* infections

In a discussion, RODRIGUEZ-MOLINA briefly reviews the therapeutics of schistosomiasis He emphasizes that in evaluating the results of therapy, false negative stool results may be found in the first month after treatment, probably because of "a temporary inhibitory action on the ovipositing females" on the part of the drug Stool examination should therefore not be made until a month has passed  
H J O'D Burke-Gaffney

BLAIR, D M Schistosomiasis in Southern Rhodesia. Public Health Aspects  
South African Med J 1948, July 24, v 22, No 14, 462-7 [12 refs]

In Southern Rhodesia schistosomiasis has been reported since 1914, and since then there has been abundant proof that infection is widespread in the country Both *Schistosoma haematobium* and *S. mansoni* are found, and since 1931 the urinary infection rate has been 2.4-4.9 per cent for Europeans, 18.5-26.7 per cent for Africans, the rates for intestinal infections were 2.1-3.8 and 10-15.6 per cent for Europeans and Africans respectively The African figures relate to hospital patients, and to that extent are selected Blair admits that it is not known if the incidence of schistosomiasis is actually increasing, or whether increased awareness is leading to increasing investigation, but his own impression is that there is an increase of schistosomiasis in all sections of the community, and that it is serious Although it is difficult to assess the importance of the disease as an ultimate cause of mortality, there is little doubt that it causes much illness, and it is regarded as one of the two major problems of public health, the other being malaria Study of schistosomiasis has been pushed on, in spite of the war

Attack may be made on the worm, or the snail, at various stages In the human host treatment can be given which is reasonably effective, the intensive course instituted by ALVES and the author is now well known In field work diagnosis presents difficulty, and the author shows that many cases may be missed if reliance is placed on a single microscopic examination of urine or faeces There has recently been an increasing tendency to perform diagnostic cystoscopy, or to take biopsy specimens from the rectum, but even these methods will not reveal all cases, and for diagnosis on a large scale they are not

practicable. Blair describes the antigen for skin testing prepared from cercariae and used on a large scale by Alves and himself [see this *Bulletin* 1947 v 41 828]. The specificity of the test seems to be good and the results have shown that 50-60 per cent. of the African population are positive. In one half of these cercariae are found in the excreta. The preparation used for intensive one-day treatment is sodium antimony tartrate and the author has no doubt that it is better to use this than the potassium salt.

Prevention of contamination of streams is of course difficult and little progress has been made, but the attack on the snails is now perfectly feasible. The author uses an empirical dose of 15-20 parts of copper sulphate per million, sprayed in strong solution or broadcast as a powder or dissolved from a sack dragged through the water. Much remains to be learned about the best conditions for treating water and about the snails themselves. The rival claims of fish culture and snail destruction may need to be balanced but in Egypt copper sulphate is used up to 50 p.p.m. without detriment to fish. Naturalistic methods of controlling snails have been suggested but cannot be relied upon.

Irrigation works and water storage dams should be planned from the beginning, with schistosomiasis in mind: the tendency to disregard it until a large snail population is established and human cases have occurred is obviously bad and a proper scheme of water management should be instituted at the outset.

Blair makes the point that *Planorbis pfeifferi* has a restricted and selective distribution yet *S. mansoni* cases are much more generally distributed. *Bulinus tropicus*, the intermediate host of *S. haematium* in Egypt, has never been found infected in Southern Rhodesia. (Darius (this *Bulletin* 1947 v 29 408) gives *B. levis* as a host of *S. mansoni* and *B. levis* (synonym *concoloratus dybowskii* (nassae)) as a host of *S. haematium*.) Such matters need and are receiving attention.

Cercariae are killed by modern methods of water purification but can penetrate filter and withstand a dose of chlorine which kills bacteria: moreover they can live 100 hours in winter so that storage of water for 48 hours is not the safety measure it was once thought to be. Protection of water is partly a matter of construction of wells and abandonment of the use of earthen dams for domestic supplies or for bathing. But of course this is extremely difficult.

[This is a succinct and readable account of the measures taken to control schistosomiasis in Southern Rhodesia. For other papers by ALVES and BLAIR see this *Bulletin* 1948 v 43 344 752 1947 v 41 828 827 829.]

Charles H. Mack

ABBOTT R. T. *Handbook of Medically Important Mollusks of the Orient and the Western Pacific*. Bull. M. Comm. Compar. & Zool. Harvard Univ. 1948 Apr. 100 No. 3 745 328 14 text figs. & 3 pls. 20 refs.]

Relatively few molluscs act as intermediate hosts for trematodes parasitizing man and all those of medical importance belong to the fresh-water Gastropoda. Nevertheless, very parasitologist interested in trematode infections, but lacking the specialized training of a malacologist has experienced difficulty when working in the tropics in identifying the comparatively few medically important species occurring in this group and has usually had to rely on sending home his specimens for identification by the expert.

Dr. Tucker Abbott has left the Orient to identify the snail on the job. Indeed the book does much of this also when returned from the field (x the 3 text of

# Helminthiasis

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identification recommended is based on the study of the external characteristics of the living snail as well as on the differentiation of shell characters and, when necessary, a study of the teeth in the radula.

In so brief a handbook—there are only about 100 pages—and one intended for the use of the medical parasitologist, emphasis is, of course, placed on those species which have been implicated as carriers of human disease, but harmless species likely to be confused with their dangerous relatives are carefully described.

Having dealt with the gross anatomy, the shell, and the radula in sufficient detail to enable the tyro to recognize the anatomical landmarks necessary for the identification of species, the author then lists the molluscan carriers of the trematode diseases of man.

The next and most extensive section of the book, consisting of 52 pages, is devoted to a systematic account of the medically important Gastropoda, although, as already noted, it includes brief accounts of species likely to be confused with known vectors. In connexion with the recognition of the molluscan carriers of *S japonicum*, the author writes "In examining dozens of genera and hundreds of species of Pacific and Asiatic fresh-water mollusks over a period of eight months in the field, it was found that all snails capable of carrying *Schistosoma japonicum* cercariae possess these characters: 'Animal with and that no other species of mollusks possess the following animal characters: two slender gray tentacles with a color-streak or "eyebrow" of bright yellow, closely-packed granules embedded in the skin just above the tiny black eyes.' It would be interesting to know whether a similar grouping of molluscs susceptible to infection with *S haematobium* and *S mansoni* can be shown to exist in other parts of the world. Although this section of the book is entitled a systematic account, it contains much valuable information concerning the ecology, habits, and distribution of the more important species.

The hosts of *S japonicum* are given as follows —

- Oncomelania quadrasi* Moellendorff
- Oncomelania formosana* Pilsbry and Hirase
- Oncomelania nosophora* Robson
- Oncomelania nosophora slateri* Bartsch
- Oncomelania hupensis* Gredler

The last seventeen pages of the book are devoted to (a) a brief account of the poison cone shells, (b) the technique of collecting and handling infected snails, (c) methods of rearing *Oncomelania* in the laboratory, (d) the control of the intermediate snail host, and, finally, two appendices, the first of which deals with a generic discussion of *Schistosomophora*, *Katayama* and *Oncomelania*, and the second with the revision of the molluscan names appearing in textbooks on parasitology.

This book will form an essential part of the equipment of all workers who are interested in trematode infections of man in the Orient and Western Pacific, and it is to be hoped that its publication will encourage the production of a similar handbook intended for the use of workers in Africa.

R M Gordon

ABBOTT, R T A Potential Snail Host of Oriental Schistosomiasis in North America (*Pomatopsis lapidaria*) Proc U S Nat Museum Wash 1948, v 98 No 3222, 57-68, 14 figs (12 on 2 pls) [14 refs]

STUNKARD [this Bulletin, 1947, v 44, 432] tested certain North American snails for capacity to act as intermediate hosts of the schistosomes of man, and obtained some evidence that *Pomatopsis lapidaria* is capable of acting as intermediate host of *Schistosoma japonicum* up to the sporocyst stage [In th

abstract of Stunkard's paper referred to above it is wrongly stated that the experiment was conducted with *S. mansoni*.]

The author describes this snail in detail, and shows on a map the 170 places in the United States from which it has been reported. There are few differences in morphology between the genera *Pomatiopsis* and *Oncomelania* and the fact that *P. lapidaria* is a host of *Paragonimus kellicotti* in North America and *O. nosophora* a host of *P. westermanni* in China (CHAN Nat. Med. J. China, 1941 v 27 550) may indicate that the two snails have a similar physiological constitution.

Charles B. Shultz

BRACKEN M. M., BAILEY W. R. Jr & THOMAS, H. M., Jr The Lesions of *Schistosomiasis Japonica*. *Amer J Path.* 1948, May v 4 No. 3 811-23 8 figs. on 3 pls. [18 refs.]

The clinical picture of acute *Schistosoma japonicum* infection among American troops in the Philippines has been widely described. A description of the lesions in man during the acute stage is largely lacking. Death is unusual in the acute stage of the disease but material was available from autopsies performed over seas on three American soldiers suffering from early eastern schistosomiasis. Biopsy specimens from acute lesion in the rectum, liver and skin of other patients were also available and there was material from cerebral lesion in Army personnel returning to the U.S.A. Specimens from older lesion were obtained from three Filipinos who died of gun-shot wounds.

The histological changes of schistosomiasis in man resemble those seen in experimental infections of small animals. The lesions run a fairly uniform course varying slightly from organ to organ. The presence of an ovum at first causes an extensive cellular reaction, eosinophils predominating. Necrosis may occur in a wide zone around the ovum. Epithelioid cells appear and multinucleate giant cells envelop the ovum. These are followed by lymphocytes and plasma cells. Fibroblastic and capillary proliferation develop in the periphery of the lesion which ultimately fibroses. The ovum becomes shrunken and calcifies in a dense fibrous tissue mass with moderate lymphocytic infiltration.

A. R. D. Adams

ESKOLA, O. On the Amount of Urobilin excreted in Urine and Faeces in Pernicious Tape-Worm Anaemia and its relation to the Reticulocyte Crisis. *Ann. Med. Intern. Fennic.* 1948 v 37 No. 1 1-15 25 figs. [32 refs.]

The author states that the excretion of urobilin by patients suffering from pernicious tapeworm anaemia (due to *Diphyllobothrium latum*) has not been systematically investigated. He therefore studied it in 19 patients suffering from this form of anaemia, with 6 healthy subjects as controls. A complete blood picture was first obtained. The tapeworms were then expelled with filicium and Epsom salts. Three days were then allowed to eliminate the effects of the filicium on the liver. The amounts of urobilin excreted in the faeces and urine during each 24 hours were then determined by the spectrophotometric method of HEILMEYER, and HARRIS (*Biochem. Ztschr.* 1931 v 231 307) and also by the reduction method of TERWIN (*Dtsch. Arch. Klin. Med.* 1925, v 149 72). [In text given as Terwin.] Each morning during the tests the reticulocytes were counted. The diet of the patients was kept as uniform as possible. Errors due to the following causes were as far as possible eliminated: disorders of the liver, organic heart diseases, infections likely to cause hepatitis, haemolytic conditions likely to cause increased excretion of urobilin, extra oxidation of blood, diarrhoea, acid fermentation in the bowel and abundance of chlorophyll in the faeces.



The results obtained with the 6 healthy and 19 anaemic subjects are described and illustrated with graphs. The author concludes that the urobilin excreted by the 6 healthy subjects during 24 hours was 75 to 180 mgm in the faeces and 0.4 to 2 mgm in the urine.

The urobilin excreted by the anaemic patients generally increased before liver treatment, it varied between 200 and 540 mgm. in the faeces and between 2.5 and 10 mgm in the urine during the 24 hours. After adequate liver treatment the urobilin excretion rose in all the anaemic patients, rising in one patient to 1,040 mgm in the faeces and 36 mgm in the urine in 24 hours, after which it fell to normal.

This increase of urobilin after liver treatment seemed in these cases to last 10 to 19 days, with an average of 14.8 days, starting one or two days after the rise of the reticulocyte count and ceasing in 2 to 5 days, with an average of 3 days, after the reticulocyte response. The author thinks that this suggests that the haemolysis is a secondary factor in the genesis of pernicious tapeworm anaemia, because the signs of haemolysis vanished with the improvement in the bone marrow which followed the liver treatment. The maximum of urobilin excretion was reached slightly after the reticulocyte peak and from then onwards slowly decreased. For reasons given in the paper, the author concludes that the time required for the urobilin to rise and become normal again represents the life-span of the megalocytes, and he concludes that this life-span is 7-14 days.

G. Lapage

BASNUEVO, J. G. Teniasis y estaño (II). [Tin in the Treatment of *Taenia saginata* Infestation.] *Rev. Kuba Med. Trop. y Parasit.* 1948, June, v 4, No 6, 119-21. English summary.

A patient who had received 16 treatments with different drugs unsuccessfully on account of infestation with *T. saginata* during 24 years, was given, by the author tablets containing the metal and salts of tin, each containing powdered tin 0.25 gm, tin protoxide 0.04 gm and the chloride 0.001 gm. He was given 10 tablets (which he calls Solitaricide Kuba) on each of two successive days and he passed a tapeworm 7 metres in length. The scolex was not found, but 14 months later neither ova nor proglottides had been seen in the faeces. Ten patients were treated in this way and 6 were cured. Later, the following was the scheme of treatment. A saline purgative the evening before, next morning, 5 tablets before any food was taken, and 5 more every half hour till 20 tablets had been taken in all. Six hours later light food was given and at bedtime that evening a purgative. During the ensuing 4 days 5 tablets are taken daily, making 40 altogether. For children, the dose is 1 tablet for each year of age up to 10, over 10 years the same dosage as for adults, and for the 4 following days 1 tablet for every two years of age.

Seven patients were treated by the 40 tablet method, 3 were certainly cured, 3 were apparently cured. For three months later examination revealed no signs of infestation. In none was the scolex found and it is thought that, though the worm is killed, the scolex has clung to the mucosa and does not pass out with the faeces. [See also this *Bulletin*, 1948 v 45, 921.]

H. Harold Scott

SWIERSTRA, D. Enige mededelingen over echinococcosis. [Observations on *Echinococcus* Infection.] *Tijdschr. v. Diergenesesk.* 1948, Aug 1 & 15, v 73 Nos 15/16 640-45.

The English summary appended to the paper is as follows —  
(1247)

"The author gives a short description of some problems and diagnostic methods about echinococcosis for veterinarians. Literature gives little information about the duration of life of *Echinococcus granulosus* in the intestines of dogs.

The opinion of Tenhaeff en Ferwerda was that the duration of life was three months.

"Some diagnostic, especially differential diagnostic methods in relation to *C. tenuicollis* are mentioned."

DELL, D. G. & MUKASA, S. B. H. A Case of Hydatid Disease of the Liver. *East Africa M d J* 1948, July v 25, No. 7 288-9.

The first case to be reported from Uganda.

MILLER, D. & FLEMING, J. Intrahepatic Hydatid Disease with Report of a Case. *Australia & New Zealand J of Surgery* 1948, Apr., 17 No. 4 291-d. 3 n.s.

ORDENAN, J. J. Parasitismo humano por *Dipylidium caninum* (Linneo 1758). [Human Infestation by *Dipylidium caninum*] *Rev. Cuba M d T p* v 1 fasc. 1948, July v 4 No. 7 143-5.

The English summary appended to the paper is as follows —

History is reported of an infant, 8 months old parasitized by *Dipylidium caninum* (Linneo 1758) apparently without symptoms. The worm is acuated by means of oral administration of both garlic and santonine. Considering the form of observation the share of each remedy in the success of the treatment cannot be determined."

BALMPT, L. C. & GUJAR, B. J. The Treatment of Polycythemia by Artificial Infection with *Leishmania donovani*. *Indian M d Gaz* 1948, Apr. 83, 4 106-9.

PASSON, W. & BARBOSA, V. de C. "Syngamus laryngeus" na espécie humana. [Human Infestation with *Syngamus laryngeus*.] *Rev. Brasileira Med* Rio de Janeiro 1948 May v 5 No. 5 340 1 fig.

A woman 45 years of age complained of a dry, obstinate cough of three months duration. On examination of her throat a small red spot was seen which was thought to be a foreign body, a fragment of coloured cotton and the patient was asked if she was in the habit of biting off her cotton when sewing. To the examiner's surprise the spot was seen to move and a worm was extracted which proved to be *Syngamus laryngeus*, a genus occurring in sheep, cattle, goats and birds, but exceedingly rarely in man. The symptoms cleared up at once and have not recurred. No upermin is offered as to the mode of acquisition of the parasite in this case. H. Harold Smith.

ALLEN, H. W. Een geval van *ascaris lumbricoles* in de tuba. [A Case of *A. lumbricoles* in the Fallopian Tube. *Nederl. T. d. Ich. & Ginek.* 1948, Sept. 4 v 92 (iii) No. 36 2758-8.

The English summary appended to the paper is as follows —

"Description of a case of *ascaris lumbricoles* in the right Fallopian tube in all probability the worm had left the intestine via the appendix.

The remarkable thing about this case was the cyclic course of the symptoms which stretched over a period of four months and the close connection of the symptoms with the menses."

NAJI, K Intestinal Obstruction due to Ascariasis Report of a Case *Lancet* 1948, Sept 25 495

LAPÉYSSONNIE L Un cas d'asthme d'origine ascaridienne [A Case of Asthma caused by *Ascaris*] *Bull Méd de l'Afrique Occidentale Française* 1947 v 4, No 3 211-14

PINTO, A R & DE ALMEIDA, C L Contribuição para o estudo das filariasas da Guiné Portuguesa. [A Study of Filariasis in Portuguese Guinea] *An Inst Med Trop Lisbon* 1947, Dec, v 4, 59-89, 25 figs (1 folding map) [14 refs] English summary

In this study the authors had in view (1) Investigation of the details of the periodicity and of the proportion of persons infested among those with elephantiasis and those infested who presented no objective signs, (2) Identification of the transmitters, (3) Study of the clinical aspect and the incidence by age and sex, (4) Finding out what filariae other than *Wuchereria* were present and to what extent, in the district. A line map indicates the district investigated and photographs illustrate the terrain and the dwellings and patients showing enlarged glands, especially in the groin, and various stages of elephantiasis of the legs and scrotum

A list of the chief diseases met with during examination of 6,227 Africans gives 134 with conjunctivitis, 130 with urinary schistosomiasis, 68 with enlarged glands, 64 with scabies, 40 with umbilical hernia, 34 with leprosy, only 28 with hookworm, and 21 with sleeping sickness. Blood samples were taken at night from 986 of different ages and either sex, whether they did or did not show signs of filarial infection, 485 (49.2 per cent) had filarial embryos in their blood. Of 172 positive who were examined again 130 had microfilariae in both day and night specimens, 42 in night specimens only. Five patients had their blood taken every two hours and the peak was seen to be between 10 p.m. and 2 a.m. Subjects with no objective signs harboured microfilariae in their blood more than those with signs, in a proportion of 7 to 5 (68 and 47 per cent), only 20.6 per cent of those with elephantiasis were blood-positive. *Anopheles gambiae* seemed to be the chief vector—it was by far the commonest mosquito, 95 per cent of nearly 2,000 captured, *Culex fatigans* only 2.5, *Aedes aegypti* 0.1 and *Taeniorhynchus* sp. 1.4 per cent, only one of *C. fatigans* was found infected, but 5 of the 28 *Taeniorhynchus*.

At all ages from infants to old people, enlargement of the epitrochlear glands was the commonest sign (between 58 and 70 per cent) and, next, inguinal adenitis in 29 to 40 per cent. Elephantiasis was not very common, in some districts only 1 per cent of the infested, and in none over 10.2 per cent.

As regards other filariae, 1,154 specimens of blood were examined for *Acanthocheilonema perstans* and the embryos were found in 36 (3.1 per cent), 28 were among 460 preparations from males (6 per cent), but only 8 among 658 females (1.2 per cent).

H Harold Scott

GALLIARD, H, HUARD, P & NGU, D V Recherches sur la filariose a *Wuchereria bancrofti*. Effets de l'intervention chirurgicale et de l'extirpation des filaires sur le rythme de la périodicité et sur la persistance des microfilaries [Effects of the Extirpation of *Wuchereria bancrofti* on the Rhythm of Periodicity and Persistence of Microfilariae] *Ann Parasit Humaine et Comparée* 1947, v 22, Nos 5/6, 332-44, 6 figs

The phenomenon of periodicity appears complex judging by the number of hypotheses which have been formulated—mechanical, physiological and biological—as affecting the host-parasite association.

The presence of great numbers of patients with filariae in Haiphong served to stimulate research on the effects of surgical operation upon periodicity but special attention was directed to the influence of castration of female filariae upon the numbers of circulating microfilariae. The serious nature of the operation precluded the carrying out of periodic daily blood examination but nevertheless curves were worked out from counts of microfilariae 2-4 days before and 3 days after operation and thenceforward at stated intervals. In every case a count was made at 11 a.m. and again at 11 p.m. The eight patients were all males and were suffering mostly from filarial disease of the genital organs.

In the first case a general anaesthetic was administered but no operative procedures were undertaken but neither the rhythm nor the periodicity of the microfilariae (*brucei*) was disturbed.

In the second, radical cure for hernia brought about a diminution of the curve and retardation for twenty four hours, but with complete restoration to its former level on the fourth day. The third was rather a similar case and a modification of the curve ensued, with delay of the maximum peak, but without any reduction in the total number of microfilariae.

In the fifth case (bilateral orchid-epididymitis with fistula) five living female filariae were recovered, after which cessation of periodicity was noted with gradual return to normal nocturnal rhythm 18 days after operation.

In the sixth (hydrocele of six years' duration) ten female filariae were found in lymphatic varices and in the eighth with a similar affection six were recovered. In case seven no adult filariae were found, but after epididymectomy the count was reduced for 4 days.

These three latter were especially important because a primary alteration of rhythm was most marked. In case 6 the maximum peak was postponed for four hours. In number 8 a diminution of microfilariae was noted within two hours on the evening of the operation, but with a return to normal on the 16th day. In one case only (5) there was complete disappearance of microfilariae for 12 days, but with ultimate restoration of the level recorded before operation.

Thus it will be seen that operative interference whether entailing destruction of a number of parturient females or not, exerts no effect upon the number of microfilariae nor upon their periodicity.

Estimations upon the blood eosinophilia failed to show any effect upon the percentage of these cells.

General anaesthesia by itself appears to be incapable of producing even a temporary depressing effect upon the microfilarial curve. Destruction of a considerable proportion of the total number of adult female filariae even if the patient is in a state of hyperfilariaemia has only a negligible effect upon the total circulating microfilariae and this certainly presents an a puzzling puzzle. Finally it seems that surgical shock and physiological disturbance are capable of exerting the most immediate and prolonged dislocation of microfilarial rhythm.

P. M. U. R. R.

MAZZOTTI L. Resultados neg. triv. de la admisión a sero del Hst. asan. en dos pacientes infectados con *M. monstrosus* asad. Negative Results (in the Administration of Histamine to Patients Infected with *M. monstrosus* asad.) *Univ. de Mexico* 1948, J 15-5 28, No. 504, 317-18.

HERMANS A. G. J. Onderhuidse gelezen, vroege door *Flavobacterium* (Oncocercus) vultus. Subcutaneous Nodules due to *O. vultus*. *Nederl. Tijdschr. Geneesk.* 1948 Aug 23 v 92 (III) No 35 2nd-8 4 tab. (1 col. pl.) [Ref. in *Lancet*.]

The English summary appended to the paper is as follows —

" In subcutaneous ulcers of a 45 year old woman patient specimens of *Filaria volvulus* (*Oncocerca volvulus*) were found. The patient appears to have been infected in tropical West-Africa.

" Symptomatology, diagnosis, occurrence and treatment of oncocerciasis as well as the observations known from literature are discussed "

DEJOU L. Kystes suppurés et abcès chroniques par vers de Guinée.  
[Suppurating Cysts and Chronic Abscesses caused by Guinea Worms]  
*Bull Soc Path Exot* 1948, v 41, Nos 3/4, 200-202

Cysts caused by guinea worms can develop slowly and like cold abscesses. They may be all the more difficult to diagnose because they may develop in patients who have never expelled a guinea worm or have done so only several months or years previously. The author records three cases which illustrate this statement, one of his own and one presented by each of two other medical men.

The first patient, aged 20, was admitted with a diagnosis of a teno-synovial cyst on the posterior aspect of the lower third of the right forearm. It was a large, fluctuating, cold, painless swelling, adherent at its base, which had developed during the past year after fever and headache, but had never been painful. Puncture of the swelling yielded thick, sterile pus containing polymorphonuclear cells and lymphocytes. Dissection revealed a sac adherent to the superficial aponeurosis of the limb. The sac had two walls, the histological features of which are briefly described. In the pus a fragment 10 cm long of a degenerate and partly calcified guinea worm was found. No microfilarial larvae were discovered.

The second patient, aged 40, had a similar swelling of the anterior aspect of the right forearm, but this was covered with oedematous and infiltrated skin. The swelling had developed in two months and it obstructed the movements of the fingers, which were in a state of irreducible flexion. This swelling went deeper and from it came abundant pus in which were found a fragment of a flattened guinea worm and immobile microfilariae. The patient had expelled numerous guinea worms several months earlier.

The third patient, aged 25 years, had a swelling at the level of the left spermatic cord and had suffered from total impotence for six months. The cyst was removed and three weeks later the patient experienced erections. The histological structure of the wall of the cyst is described. In the cyst was an almost intact, but apparently dried up, guinea worm.

G Lapage

## DEFICIENCY DISEASES

- 1 BLANC, F & SIGUIER, F. A propos de 8 cas de pellagre observés au cours de dysenteries ambieuses chroniques [Eight Cases of Pellagra in Patients with Chronic Amoebic Dysentery] *Bull et Mém Soc Méd Hôpit de Paris* 1947, Nos 23, 24 & 25, 630-36

- 11 — & — Les pellagres post-dysentériques [Post-Dysenteric Pellagra] *Ibid* 636-42 [Refs in footnotes]

1 In two patients with chronic amoebic dysentery there was a sudden onset of painful erythema of exposed parts, with aphthous stomatitis and mental symptoms—irritability and depression. Rapid relief was produced by a single injection of nicotinamide (250-500 mgm). The response to treatment, together

with the clinical findings suggested a diagnosis of pellagra. Brief mention is made of six other cases of amoebiasis, in which erythema of the limbs or aphthous stomatitis were cured by nicotinamide.

ii. Since in none of the cases was there a history of a deficient diet the pellagra was attributed to malabsorption. All the patients suffered from chronic and severe diarrhoea, with 15 to 30 stools a day. This did not respond to nicotinamide but was relieved by anti-amoebic treatment. In spite of the diarrhoea the patients were generally well nourished, and showed no signs of deficiency states other than pellagra. It is suggested that, in order to avoid this complication, patients with amoebic dysentery should be given a good mixed diet, and not a severely restricted one.

J. C. Hatcher

GOUXELLE H. Pellagre et carences d'apport. [Pellagra and Contributory Deficiencies.] *Bull. et Mém. Soc. Méd. Hôp. de Paris* 1947 Vol. 30/31 911-14 [1<sup>st</sup> refs.]

The authors refer to the papers by Blanc and Siguer (above) and suggest that deficiency of nicotinamide may not be the sole cause of pellagra. During the war they studied an epidemic of pellagra occurring among the inmates of an institution, and compared the diet of the patients with that of the average citizen of Paris. The institutional diet contained slightly more nicotinamide than that of the Parisians but less fat and animal protein (see also MONTAIGO *et al.*, this *Bulletin* 1947 v 44 340. ATKINSON and SWAMINATHAN *ibid.* 1940 v 37 97).

Such observations suggest that deficiency of amino-acids as well as of nicotinamide may play a part in the genesis of pellagra. This view is supported by the demonstration, both in experimental animals and in man, of a metabolic relationship between nicotinic acid and tryptophan (FRIEDBERG *et al.* *J. Biol. Chem.* 1947 v 167 511. LEECKE *et al.* *J. Nutrition* 1947 v 33, 251. BRENN *et al.* *J. Biol. Chem.* 1948, v 162, 403).

J. C. Hatcher

## HAEMATOLOGY

GINDWOOD R. H. Anaemia and Marasmus in Indian Troops on Active Service. *Trans. Roy. Soc. Trop. Med. & Hyg.* 1948, July 42, No. 1 63-82 [22 refs.]

An investigation into the cause of anaemia and marasmus among Indian troops was started in the early part of 1945. The haemoglobin percentages of the bloods of 500 Indian soldiers passing through a transit hospital in Bengal were ascertained. The mean of the group was 14.17 gm. per 100 ml. 7.4 per cent. were below 8 grammes and 11 per cent. below 11 grammes. There was no significant difference between the meat-eaters and the non-meat-eaters, nor between groups arranged according to length of service with the exception that those with less than a year's service had only 11.89 gm. per 100 ml. which was significantly lower than the rest. However this group was almost entirely composed of men from a Pioneer unit which had a strikingly low mean haemoglobin percentage.

During July 1945 83 cases from east of the Brahmaputra river were admitted to a special anaemia centre. Stool examinations for a were carried out by a concentration method in 61 cases, and in 35 (41 per cent.) ancylostomiasis was found (weight of infection not stated). The mean haemoglobin concentration of the 35 patients with hookworm infection was significantly lower than that of those with no ova in their stools.

One hundred and twenty-four Indian other ranks suffering from the marasmus syndrome were investigated. The haemoglobin findings in 27 are reported. All but one came from east of the Brahmaputra river and the average duration of symptoms was 17 weeks. Data regarding food supply was unsatisfactory. 84 of the group were meat-eaters, but supplies of fresh meat were negligible in the jungle areas. Most of them had had malaria, a record of the finding of parasites was obtained in 51 cases, and all but 6 had received mepacrine regularly. "There was nothing in the history of these men to suggest that either bacillary or amoebic dysentery played a part in the onset of their illness." Stool examinations in 88 cases revealed ancylostome ova in 27, *E. histolytica* (vegetative form) in 4 and cysts in 1, other protozoa and helminths were found, but 44 cases were negative.

The commonest clinical features were diarrhoea (83), flatulence (75), anorexia (70), abdominal pain or discomfort (69), vomiting (60), fever (44), glossitis, marked evidence of loss of weight (52), palpable spleen (33), and marked dryness of skin (33).

"According to the findings of the absolute indices, the distribution of the types of anaemia in the cases under consideration was as follows: orthochromic macrocytic, 17; hypochromic macrocytic, 8; hypochromic orthocytic, 2."

Megaloblasts indistinguishable from those found in pernicious anaemia, except that haemoglobinization of the intermediate megaloblasts was less advanced, were found in the sternal marrow in 62 out of 96 cases. Many patients had shown resistance to treatment with crude liver extract by intramuscular injection in their previous hospital treatment. In some of these cases megaloblasts still persisted. Liver injections, with the addition of mepacrine therapy, were given in 8 cases, significant improvement only occurred in 2. The liver injections, however, appeared to precipitate an attack of malaria in each of five of these cases. Neither folic acid nor protolysed liver was available at the time of the investigation.

The author gives no "conclusions", nor in the "summary" is there any expression of opinion on the aetiology of the condition. The following quotation might possibly be taken as his tentative opinion on the aetiology of the anaemia, but it appears to have little connexion with the data he has presented —

"It is evident that the anaemia described in the present series of cases is of a very complex type. Possibly years of primary malnutrition prior to joining the Services played a part in many cases, and was aggravated more recently by supply difficulties during jungle fighting. Thus there might be a deficiency of Wills's factor, and conceivably of extrinsic factor, which would give a tendency to megaloblastosis. In addition, there was a sprue-like condition, which itself might induce a megaloblastic form of anaemia due to malabsorption of the liver factor produced by the interaction of Castle's extrinsic and intrinsic factors, or of folic acid conjugate (Davidson, and Girdwood, 1947). To what extent prolonged low intake of protein of high biological value plays a part is unknown."

"Malarial infection, when present in men suffering from such a deficiency syndrome, might add a haemolytic element, and thus increase the megaloblastosis in the manner described above."

L E Napier

AIENGAR, N A, NAIDU, B R L, KRISHNAMURTHY, C B & RANGANNA, B  
**Observations on Anaemia in the Malnad Parts of the Mysore State** *Indian Med Gaz* 1947, Aug, v 82, No 8, 488-93, 10 figs on 1 pl

"Anaemia associated with nutritional deficiencies, malaria and hookworm disease is severe and widespread in the Shimoga and neighbouring districts of

Mysore where the average diet appears to be extremely poor in protein and fat. Some 2,000 patients were studied in hospital during four years, and approximately one third of the patients had total erythrocyte counts of less than 14 million per cmm. Treatment consisted initially of liver extracts, iron and quinine. Vermifuges were given later when the patients' condition had improved. The results of such treatment appeared disappointing, and the real remedy would seem to lie in fundamental measures to raise the standard of living and of education in the affected regions. *F. Margatroid*

BAUER, J. Sickle Cell Disease. Circulatory Stasis in Small Blood Vessels. *Acta Med. Scand. navaica*. 1947 Oct 15 v 129 No. 1 111

This paper contains nothing new but emphasizes that the important pathological process in sickle cell anaemia is the circulatory stagnation caused by deformation of the erythrocytes, which produces haemolysis, thromboses, and ischaemia of the tissues with later endarteritis and fibrosis in the affected area. *F. Margatroid*

### VENOMS AND ANTIVENENES

DEL POZO E. C. The Action of the Venom of a Mexican Scorpion (*Centruroides noxius* Hoffmann) on Cholinesterases. *Brit. J. Pharmacol. & Chemotherapy* 1948 Sept., v 3 No. 3, 219-220, 1 fig

"The effects of extracts of the venom of a Mexican scorpion (*Centruroides noxius*, Hoffmann) were examined on cholinesterase preparations with the view of finding out if the curarine-like effects this venom exerts on isolated tissues and in animals on intravenous injections could be explained by a cholinesterase inhibiting property. The venom extract was only found to inhibit pseudoe as well as true-cholinesterase when present in very high concentrations. It is concluded that the symptomatology of the venom poisoning is independent of or dependent to a very slight degree only on inhibition of cholinesterase

DE MAGALHÃES, O. Combate ao escorpianismo. Nota prévia. (Dealing with Scorpions.) *Bras. de Medicina* 1948, Apr 17 & 24 v 62, Nos. 16/17 109 U.

The author describes the results of Gammaxane on scorpions in Brazil, notably the *Tityus bahiensis*. The substances used were the fluid LG-140 which contains 10 per cent. of the gamma isomer by weight and is diluted 1 in 30 with kerosene or the powder D-4034 (which contains 0.5 per cent. of the isomer) 1 gm. emulsified in 30 gm. of kerosene. After contact for 1.5 minutes the scorpions die in 20 minutes or so. The symptoms seem to be in three phases. In the first, though poisoned they show nothing definite, then they become very excited and agitated, running from one side of the containing box to the other, tails erect and striking at everything within reach around them. This is followed by the third phase of ataxia and paralysis in which they run about in a disorderly manner, are ataxic with generalized tremors or move in small circles before becoming paralyzed. Gammaxane should prove very serviceable in dealing with dangerous scorpions in Brazil. *H. Harold Smith*

AMERICAN MED. 1948, July v 5 No. 4 54-61 Modern Treatment of the Bites and Stings of Small Desert Animals.

(This is a sort of Brains Trust on medical problems, or a 100 reply to the Any Questions section of the *British Medical Journal*. An actual case is



recorded and a team of six, whose qualifications to reply are detailed, is named, each member of which expresses his opinion on the diagnosis and treatment.]

A child of 8 years was bitten on the ankle by something unknown. He was taken to hospital and 30 minutes after infliction of the injury there was an area of redness 2 inches above the right ankle and a single indistinct puncture wound, but no discoloration. The child was conscious, nervous and restless [in fact, there seems to have been little wrong and much of the child's symptoms might have been due to parental panic]. The members of the panel gave their opinions in turn, taking into consideration scorpion sting, spider bite, especially *Latrodectus mactans*, a small rattlesnake, a centipede [with a single puncture?], tarantula, Gila monster, coral snake, bee, wasp, or red ant sting. The treatment of each of these—first aid by a tourniquet, local application of cold, incision (if no doctor is near), stimulants for shock, and specific treatment by antivenenes and anti-histamine drugs—is stated by different members of the team, but in rather general terms. [The principle of the series is that any doctor confronted by a difficulty can send it up for discussion by specially chosen consultants. If urgent, a reply is sent direct, without waiting for publication.]

H Harold Scott

## DERMATOLOGY AND FUNGUS DISEASES

MORTA, L da C Paracoccidioides Granulomatosis Cardiac Localization in a Case of Generalized Form *Amer J Path* 1948, Mar, v 24, No 2, 323-37, 12 figs on 3 pls [20 refs]

The author gives a fully documented account of the history and nomenclature of the fungus *Paracoccidioides brasiliensis* (Splendore) Almeida 1930, followed by a discussion of the clinical features of the South American and North American types of blastomycosis, which are clearly differentiated from each other. He points out that the cutaneous lesions in the South American disease are invariably secondary, and are due to dissemination of the fungus from some deeper focus. He agrees with other observers that the primary lesions occur on the bucco-pharyngeal mucosa in the form of granulomatous ulcerations frequently of a papillomatous or vegetative character, which indicate an oral path of infection. From these lesions the infection reaches the cervical lymph nodes and extends to the supraclavicular, axillary and other groups, constituting the "lymphatico-tegumental" form of the disease. From 3 to 18 months later a general dissemination of the parasite through the blood stream may occur, causing cutaneous and visceral lesions, which may affect nearly all tissues of the body, and death soon follows.

A detailed account is given of the post mortem examination of a case of the generalized disease in which the fungus was found in destructive lesions of the cardiac musculature, and in its actively reproductive form in the lumen of a cardiac blood vessel, indicating a "septicaemic" state. Both of these are original observations.

J T Duncan

LACAZ, C DA S, ASHCAR, H, COSTA, O & VIOTTI, M R Ação da estreptomycina 'in vitro' sobre o paracoccidioides brasiliensis, Ensaio terapêutico na blastomycose sul-americana [Action of Streptomycin *in vitro* on *Paracoccidioides brasiliensis* and Attempts to use it in the Treatment of South American Blastomycosis] *Hospital* Rio de Janeiro 1948, May, v 33, No 5, 693-703, 2 figs [10 refs]

The authors study the action 'in vitro' and 'in vivo' of streptomycin upon *Paracoccidioides brasiliensis*, agent of South-American blastomycosis

High concentrations (5,000 U. to ml. and onwards) of streptomycin inhibit growth of *P. l. anisurus* at its lag phase or phase of logarithmic growth. Lesser concentrations have no effect upon *P. brasiliensis*. The authors verified that this fungus may have an inhibitory action upon streptomycin. After the studies in vitro the authors made use of streptomycin in a case of generalized ganglionic blastomycosis. 29 gra. were employed on the whole (1.5 gra. daily). The lesions did not recede with this treatment but general conditions of patient remained stationary. The observation is drawn to a close by showing streptomycin's low therapeutic value in cases of blastomycosis. Sulphonamide preparations are still the therapeutics to be relied upon.

LITTMAN M. L., WICKER, E. H. & WARREN A. S. Systemic North American Blastomycosis. Report of a Case with Cultural Studies of the Etiologic Agent and Observations on the Effect of Streptomycin and Penicillin in Vitro. Amer. J. Path. 1948 Mar & Apr No. 2, 139-65 11 figs on 5 pls. [19 refs.]

The authors describe a case of systemic blastomycosis, of the North American type in a male negro aged 20. The signs and symptoms were mild afternoon pyrexia with night sweats and blood-streaked sputum and an X-ray picture of miliary nodules scattered throughout both lungs. These seemed to justify the diagnosis of pulmonary tuberculosis, although the tubercle bacillus had not been found in the sputum. The development of multiple tender cutaneous nodules might have suggested another disease but the onset of mental symptoms with signs of an intracranial lesion prompted the diagnosis of tuberculous meningitis. Before death however *Blastomyces dermatitidis* was found in the pus of a subcutaneous abscess.

A brief account is given of the post mortem findings, the most interesting of which was the lesion on the brain. In the region of the superior sagittal sinus the under surface of the dura mater was closely adherent to a yellowish friable mass, 2 to 1.7 mm. deep and about 3 cm. wide, consisting of a granulation tissue and inflammatory exudate of polymorphonuclears, lymphocytes, plasma cells and macrophages, with numerous spherules of the fungus *B. dermatitidis*. The brain cortex was necrosed to a depth of several millimetres over the mesial and upper surfaces of the occipital and parietal lobes, and the leptomeninges on the base of the brain, the cerebellum, pons and medulla oblongata were covered by a tenacious, thick yellowish-green exudate.

In the primary cultivation of the fungus from pus colonies were obtained on blood-agar after 4 days incubation at 37°C., but, on glucose-agar at room temperature a more typical mycelial form developed in from 7 to 16 days.

Two strains of *B. dermatitidis* were found to be resistant to penicillin and streptomycin in culture when these antibiotics were present in the culture medium at a concentration of 200 units per ml. J. T. Duncan

BRAH K. C., BRAH, G. & VERMA T. W. J. C. Localized Lesions of the Meningi and the Brain caused by a Brown Fungus with Septate Hyphae of Unknown Nature. N. I. Masnik. Batavia. 1948. J. no 1 No. 23 145-7 4 figs on 2 pls.

## TROPICAL OPHTHALMOLOGY

## A REVIEW OF RECENT ARTICLES LI\*

*Blindness*—The report on *Blindness in British African and Middle East Territories*<sup>1</sup> is divided into three parts

Part I deals with statistics of blindness, the social condition of the blind, the medical services, the causation of blindness, education of the seeing and the blind, and the training, employment and after-care of the blind

Part II deals with a scheme of blind welfare, the administrative organizations capable of giving effect to a plan of development, voluntary organizations, finance, registration of the blind, prevention of blindness, propaganda, education of the blind, vocational training, employment and Braille production

The Appendices give details of the institutions for the blind in the Colonies visited, registration, a description of a Colonial medical department, a mobile ophthalmic unit, curriculum in a school for the blind, native industries suitable for the blind, Braille printing unit for colonial use

The investigation carried out by the Joint Committee appointed by the Colonial Office and the National Institute for the Blind reveals that there is a real problem of blindness in the Colonies and that seventy-five to eighty per cent of the blindness is preventable The report suggests a scheme of prevention of blindness, treatment of blindness and the education, training and employment of the young blind This scheme can be put into operation without delay and has possibilities of wide expansion

The Report is an excellent summary of the blind problem in British African and Middle East territories, and by those interested in the subject it should be read *in toto*

The causes of blindness in *China* are discussed by FLOWERS<sup>2</sup> It is generally agreed that the incidence of blindness is high, but it is strange that so little has been written on the possible causes of this high incidence The surveys on which we are mainly dependent for evidence cover hospital out-patients in particular centres and are made by busy ophthalmologists Valuable and reliable as these are, they can only give us part of the story and cover only a short span of time

From the statistical reports of CHANG, CUNNINGHAM [*Bulletin of Hygiene*, 1937, v 12, 208], SHEN, and LING [this *Bulletin*, 1924, v 21, 459, 983] it would appear that the following diseases are the most important causes of blindness in *China*

(1) Ulcerative keratitis of unknown origin In all the reports, a high proportion of eyes are blinded by this disease Acute conjunctivitis, including the damaging muco-purulent form, is one of the most frequent eye diseases seen in the average hospital in *China* and is the original cause of most of the corneal ulcers The organisms which are most frequently found are the Koch-Weeks bacillus, the pneumococcus, and the gonococcus Muco-purulent conjunctivitis is commonly associated with trachoma, the one aggravating the other

\*For the 50th of this Series see Vol 45 pp 646-648

COLONIAL OFFICE *Blindness in British African and Middle East Territories* Being the Report of a Joint Committee appointed by the Colonial Office and the National Institute for the Blind following the visit of a Delegation to Africa and certain British Middle East Territories between July 1946 and March 1947 [HEATH D F THOMAS Mary G & WILSON J F] pp xii+99 1 fig 1948 London H M Stationery Office

Causes of Blindness in *China* *Chinese Med J* Shanghai 19

(2) Trachoma. Along with Egypt and India, China must be regarded as the home of trachoma and this disease must be considered as one of the major causes of blindness if not the principal one. A very high proportion of China population is infected with either acute or chronic trachoma which produces blindness directly from its numerous complications or sequelae or by providing the fertile soil on which more acute infections flourish. It is probably not the most important cause of blindness in the young. Its damaging effects are mainly produced in adults as a result of prolonged irritation and scarring.

(3) Phlyctenular conjunctivitis. Lung regards this disease next to trachoma, as the most common eye disease affecting young people of either sex. It often attacks both eyes and tends to recur over a period of months or years. The disease is an expression of the debilitated constitution of the patient and is mainly found among the poorer classes. In the majority of cases the Mantoux tuberculin test is positive.

(4) Syphilis. It would appear that this disease is not a common cause of blindness and that congenital syphilis is a comparatively rare disease. It is probable that in the large cities nearer the Eastern seaboard where syphilis is so widespread, it is a much more frequent cause.

(5) Keratomalacia. This disease must be regarded as one of the important causes of blindness in children under ten years of age and is due to the prevailing malnutrition resulting from war.

(6) Gonorrhoea. Many infants lose their vision from this disease as a result of delivery by untrained midwives. Credé's prophylactic treatment of instilling a weak solution of silver nitrate drops in the eyes of new born babies immediately upon delivery is not generally practised in China. Blindness in adults from acquired gonococcal infection is however much commoner than that from ophthalmia neonatorum but it is highly probable that large numbers of infants lose their sight from this cause but are never referred to hospital for diagnosis and treatment.

(7) Acute infection fevers, smallpox and measles. These diseases are probably not uncommon causes of blindness particularly in the north and in country districts but the figures produced by different writers are conflicting and the true picture will only be ascertained after fuller surveys have been carried out.

(8) Trauma. Since the large majority of China's population are agriculturalists there is comparatively little traumatic blindness.

(9) Cataract. This is probably the commonest cause of blindness in old people and a high proportion of cases are complicated by the lesion resulting from chronic trachoma.

(10) Glaucoma. This is also a fairly common cause of blindness among the adult population. In a large number of cases the disease is undiagnosed and when the patients present themselves for treatment the condition is inoperable.

(11) Hereditary and congenital defects. These are considered to be uncommon factors in the causation of blindness in west China.

The indirect causes of blindness in China may be summed up as ignorance, poverty, malnutrition, neglect of vaccination against smallpox and the lack of adequately trained midwives to safeguard the eyes of the newly born.

Surgery.—Recent advances in cataract surgery as reviewed by Gill<sup>1</sup> He advocates the following technique for the extraction of the lens in capsule. The pupil is dilated by instilling two drops of 0.5 per cent scopalamine hydrobromide in the conjunctival sac. Atropine produced by the anesthetic. A lid speculum is not used. The lid is held open by silk sutures. The upper incision is placed under the superior rectus muscle 4-6 mm. behind its insertion.

GILL, F. Cataract Surgery. Recent Advances. Southern Med J. 1948, Mar 41, No. 3, 191-2, 8 figs. [14 refs.]

The lower suture is placed through the skin of the lower lid near the lid margin. A full 180 degrees concentric conjunctival flap is dissected down 3 mm from the corneal limbus. Double-armed corneo-scleral sutures are placed at 1 and 2 o'clock with No 60 silk in atraumatic needles. Conjunctival sutures are placed at 10, 12 and 2 o'clock. The section is made at the limbus with a specially devised keratome which is 14 mm in width at its base. The incision is widened to the horizontal meridian with scissors. If an iridectomy has been decided upon, it is performed at this point. The final step in the operation is the extraction of the lens in capsule by the head-on or Verhoeff method. The zonular fibres are ruptured by point pressure at 4, 6 and 8 o'clock. Gentle pressure is made on the iris at 3 and 9 o'clock with a small iris retractor. Firm continuous pressure is made on the limbus at 6 o'clock. When the lens presents itself in the wound it is grasped by Verhoeff capsule forceps and delivered by continuous pressure from below. The sutures are then tied and 1 per cent atropine is instilled in the conjunctival sac. The patient is generally allowed out of bed twenty-four hours after operation. The author claims that by this technique 90 per cent of his cases achieved a visual acuity of 20/25 or better. Haemorrhage has been reduced to 3 per cent and vitreous loss to 2 per cent.

A new operation for entropion and trichiasis of the upper eyelids is described by MASCATI<sup>4</sup>. The technique is as follows. Before commencing the operation, the surgeon should study very carefully the arrangement of the displaced lashes and should keep in mind their position. A light scratch with a very sharp knife is made, parallel to the upper lid margin, slightly above the position of the hair follicles. The ends of this scratch should extend a little farther away than the last mal-placed hair on either side. This scratch is meant only as a mark and should not include the whole thickness of the skin. A second scratch is made below and parallel to the first and the incision goes right down to the subcutaneous tissue. A third scratch is made above and parallel to the first one so as to include a strip of skin, the breadth of which should be about 2 mm more than the distance between the first scratch and the grey line. A fourth scratch is now made exactly on the grey line, splitting it to the length of the first scratch. A tunnel is made through the split grey line up to the first scratch. The strip of skin between the first and third scratches is freed from above and at the sides, leaving it only attached to the upper border of the first scratch. All subcutaneous epidermal tissues are removed from the freed strip to make it as thin as possible. The strip is then drawn through the tunnel and stitched to the grey line with interrupted sutures. The upper edge of the third scratch is then sutured to the lower edge of the second scratch.

*Trachoma* — Trachoma in Changsha, Hunan, is reviewed by Chen-Chung Wu<sup>5</sup>. This disease is one of the common chronic diseases in China and is also one of the most important medical and public health problems, since it causes blindness either directly or indirectly. Out of 1,340 outpatients attending the Department of Ophthalmology, National Hsiang-Ya Medical College and Hospital between September 1946 and March 1947, 1,017 (75.88 per cent) suffered from trachoma. Of these cases 29.43 per cent were mild cases, 67.26 per cent were moderate and 1.31 per cent were severe cases. The highest age incidence is between 10 to 40 years. Occupational incidence ranks highest among students and teachers, then merchants, housewives, etc. Most cases are in Stage 2 (MacCallum's classification) and moderately severe. A list of common complications and sequelae is presented, and pannus heads the list. Two hundred and sixty-five of the 1,872 eyes seen were blind.

<sup>4</sup> MASCATI, N. T. A New Operation for Entropion and Trichiasis of the Upper Eyelids. *Indian Med Gaz* 1948 Feb v 83 No 2 79-81 9 figs.

<sup>5</sup> Wu, Chen Chung. Trachoma in Changsha. *Chinese Med J* Shanghai 1948 Mar, v 66 No 3 144-7 [16 refs]

**Malaria.**—Migraine due to malaria is reviewed by SÉDAN.<sup>6</sup> He reports a case which had a bilateral scintillating scotoma followed by a temporary blindness. This was accompanied by a total paralysis of the right third cranial nerve. The fundus revealed lechaemia with spasm of the retinal arteries. The veins appeared normal. The macula appeared to be more coloured than the rest of the retina, probably more in contrast than effect. The case cleared up quickly on one intravenous injection of quinine. The paralysis lasted longer than the blindness, but the eye became normal by the end of the second week of treatment.

The author considers the case worthy of publication for the following reasons. Spasm of the retinal arteries as a result of malaria is very uncommon. Its association with an ocular palsy so far as he knows, has not been reported. The action of quinine in the cure of the blindness, the headache and the paralysis was remarkably rapid and so rules out the possibility that these complications are due to quinine therapy. Although these ocular manifestations are at the time alarming the author considers they are benign and clear up on treatment.

**Leprosy.**—A case of iridocyclitis leprosa imported into Denmark is described by HANSEN.<sup>7</sup> In a man aged 41 years, who had spent 15 years in the East. He first developed a localized eruption of leprosy on the left upper arm. Four years later he developed a general eruption of the anaesthetic type and this was followed four years later by a bilateral iridocyclitis with increased tension and lepromata on the left iris. The ocular signs progressed in spite of improvement in the skin affection and the vision deteriorated. It was not possible to follow the further progress of the disease as the patient returned to the East.

The author points out that the eyes are often affected in leprosy and that these complications are serious. The cornea is the part of the eye most frequently attacked. Iritis is always found together with affections of the cornea and occurs after the cornea has been invaded. The iris may however be the seat of primary attack. The disease follows a slow relentless course with periods of improvement and exacerbation but the prognosis is grave and the presence of lepromata considered to be a special sign of the malignancy of the disease. According to some authors, lepromata may be the first sign that the disease is passing from the tuberculoid to the lepromatous form.

Disagreement prevails with regard to the way in which the infection enters. Some assume the infection to be exogenous through conjunctiva and epibclera some that it is secondary to a nasal focus, but most authors on the basis of microscopy and clinical investigation consider that the infection is endogenous with a primary lesion in the anterior part of the ciliary body and at the circulus undis major from which it spreads to the iris, sclera and cornea, while the posterior part of the eyeball is rarely attacked. E. O'G. KIRWAN

MACCHIARELLO A. El virus del tracoma y su cultivo en el saco yelmo del huevo de gallina. [The Virus of Trachoma and its Cultivation in the Yolk Sac of the Hen's Egg.] Reprinted from *Rev. Epidemiol. de Hig. y Med. Trop. Guayaquil*. 1944 Apr v 1 N. 2, 33 pp. 108 refs.

Macchiarello's experiments which resulted in the culture of trachoma virus in the yolk sac of the hen's egg can be summarized as follows. The following standard abbreviations are employed. —I.B. = Initial body, intracellular basophil, measure, 1.0—10 µ. P.H. = Prowazek-Haller-Standert body count type, 1.2 basophil, circular or oval enclosing a mass of acidophil elementary granules (E.H.). The P.H. measures more than 10 µ the E.H. 0.3 to 0.5 µ.

6. *Migraines ophtalmiques* M. Sédan. *Angewandte ophthalmologie und pathologie der Augen*. *Handb. d. Med. Trop.* [H. 15] 1946, No. 49, 163-70.

7. Kirwan, E. O'G. A Case of Iridocyclitis Leprosa. *Acta Ophthalmologica*. 1947, 25, N. 3, 263-6. [15 refs.]

(I) The source of the virus was a young man M A, aged 17, who had suffered from a disease diagnosed as trachoma for three years. When seen by the author this was in stage Trachoma II, with reddened conjunctiva and follicles. The cornea was not affected. Indigenous trachoma is not known in Ecuador although immigrants, usually Syrians, carry the disease. M.A. had not been in contact with such cases. Scrapings of the conjunctiva of M A showed the classical inclusion bodies.

Follicles removed from his conjunctiva were finely divided with scissors and emulsified in Tyrode solution. This emulsion was used unfiltered for the inoculation of seven eggs, in the yolk-sac according to Cox's method [see this *Bulletin*, 1942, v 39, 381]. The eggs had previously been incubated for 3, 6 or 9 days. On the 3rd day after inoculation, four of the eggs were examined. Three were found contaminated and were discarded, while study was concentrated on the fourth containing a 9-day embryo (*i.e.*, it had been incubated 6 days before inoculation). In films made from the wall of the yolk sac the following bodies were found: (1) Initial bodies, (2) larger basophil bodies containing acidophil granules, *i.e.*, P K, (3) rare E K, (4) free in the yolk a few vesicular P K were found. No traces of virus were found in the albumin, in the chorio-allantoic membrane or other membrane. *Cultures on bacteriological media remained sterile*. (II) The remainder of the yolk-sac of this egg was washed in broth, triturated in a mortar, re-suspended in Tyrode and divided into two halves, of which one was filtered through a Seitz E K membrane, the other left unfiltered. With each half, 8 eggs of 5-6 days incubation were inoculated.

The eggs inoculated with unfiltered suspension were found to be contaminated and were discarded.

Of the eggs inoculated with filtered suspension two were examined on the 6th day and showed a good development of virus. One was examined on the 23rd day (the embryo was then at term, having been delayed in development by the virus) and it showed abundant E K. In subsequent passages the most abundant infection was always found on the 23rd day. From this (filtered) source subcultures were made by Cox's method through 9 generations, the material being filtered if contamination appeared. The 9 generations occupied from the 5th January 1943 to the 7th March 1943.

Filtration of the emulsion of yolk-sac through a Berkefeld N or Seitz E K filter was successful if the virus had reached the stage of E K, but not if still in the plaque or morula (I B) stage. Retention was probably due to a matrix containing glycogen. [It should be noted that virus taken direct from the man M A proved unfilterable, that filterability began after infection of the egg.]

(III) Experimental transmission of trachoma from the egg to man. An emulsion of a yolk sac of the 9th passage which was rich in E K was filtered through a Berkefeld N candle. One drop of this filtrate was instilled into the eye of a boy aged 6 years. Six days thereafter there was reddening of both eyes with lachrymation and photophobia. These symptoms persisted for 3 days (from 7th to 9th) but were absent between the 10th and 14th days. On the 15th day after infection they recurred more severely and simultaneously in both eyes. The conjunctiva was intensely red and oedematous, lachrymation and photophobia were marked. Feverish reaction and diarrhoea lasting four days occurred. After the 21st day, there was considerable vascular infiltration of the cornea which appeared definitely opaque. Treatment with sulphathiazole was then carried out. At the end of two months from infection, the conjunctiva and cornea were nearly normal in appearance and after one year there was no change. Sight was perfect and there was no ptosis.

During the period of observation scrapings were taken daily from this child's eyes with the following results. From the 6th to the 10th day during

the first period of conjunctivitis, no inclusions or virus bodies of any kind were found. From the 10th to the 13th days during regression, numerous free basophil dots and a few basophil inclusions were found. From the 15th to the 18th days the conjunctival cells were filled with granules of various sizes. After the 18th there were fewer I.B. inclusions, E.h. were beginning to appear in the centre of these bodies and by the 25th day they had become typical I.h.

Three times during the acute stage, on the 8th, 16th, and 19th days, cultures into eggs were made from unfiltered and from filtered secretion. Only the unfiltered material in the last two experiments proved infective. On the 7th day both eyes were washed out thoroughly secretion was collected and filtered through a Berkefeld V and infected into 4 eggs, all of which yielded a great multitude of E.h. when examined between the 4th and 7th days.

[Dr Macchavello is to be congratulated on the very interesting results of his work. But as there appears to be some doubt whether the disease with which he dealt was identical with trachoma of the Eastern hemisphere, the experiments should be repeated.]

F. H. Stewart

SOTTA E FARO. A epidemia do tracoma no arquipelago de Cabo Verde. [Outbreak of Trachoma in the Cape Verde Islands.] *Gaz. Med. Portuguesa*, 1948 v 1 No. 1 191-5. English summary

In August, 1943, the author was sent to the island of Sal to investigate an outbreak of trachoma which had appeared among soldiers of the garrison. He found 349 cases 20 in native soldiers. Of the other 329 there were 157 in the first stage (of McCallan) 169 in the second, 3 in the third. So far as could be ascertained the first case had occurred at Praia, a town of the island of St. Iago and thence the infection had spread by manual contact by the common and promiscuous use of towels and other personal belongings, and by the agency of flies for the place was hot and dusty. The civil population could, naturally, not be isolated, but those with trachoma were confined to certain houses under supervision and careful hygienic conditions—careful washing of hands, towels, clothes, etc. restricted to personal use, keeping down flies and the treatment of patients with copper sulphate, nitrate of silver, sulphathiazole, cyanide of mercury and treatment of any concomitant disease.

H. Harold Scott

## HEAT STROKE AND ALLIED CONDITIONS

LEE, D. H. H. & MACHERSON, R. H. Tropical Fatigue and Warfare. *J. Appl. Physiol.* 1948, July 1 No. 1 60-72.

Much of the morbidity experienced in the tropics can be attributed to "peptic" "tropical diseases" but there has remained a rooted conviction that there is a residuum of morbidity directly attributable to exposure to extremes of heat and humidity and to this the term "tropical fatigue" has been applied. This so-called "tropical fatigue" assumed considerable relative importance as a cause of disability in tropical warfare and about the middle of 1944 it was decided to investigate its nature and incidence amongst military personnel serving in the Southwest Pacific Area.

It appeared that if tropical fatigue existed it might be either a physical or mental phenomenon, or a combination of both. Since psychological methods of investigation did not appear suitable for use in a field survey, it was decided to concentrate on the physiological aspects, and to treat mental aspects largely by a method of elimination.



The approach adopted was to record the opinions of commanding and medical officers as to the efficiency of personnel in relation to the length of tropical service, to measure by suitable tests their physical condition and to relate the measurements to the length of tropical service, and to estimate the importance of psychological effects by comparing physical deterioration with the loss of efficiency reported

To test cardio-vascular reactions to acute maximal exercise the Harvard Pack Test was used. The subject wears a pack weighing one-third of his body weight and steps up on to and down from a platform 16 inches high once every two seconds until he can no longer maintain the pace or until five minutes have elapsed. The index is then calculated from the quotient when the duration of the exercise is divided by the sum of pulse counts after the exercise

$100 \times \text{Duration in seconds}$

$I = \frac{\text{Twice sum of pulse beats counted 1 to } 1\frac{1}{2}, 2 \text{ to } 2\frac{1}{2}, \text{ and } 4 \text{ to } 4\frac{1}{2} \text{ minutes after cessation}}{\text{Duration in seconds}}$

It was concluded that there was a general lowering of efficiency in R A A F ground crew surveyed in tropical areas as compared with those examined near Brisbane. Beyond a slight initial loss of weight, the only objective evidence of deterioration in physical fitness was that given by the Harvard Pack Test Index which showed a net fall of 0.19 units per week of tropical service. This is a small effect but it may assume importance after 12 months or so. The index was significantly correlated with the subject's own estimate of his efficiency, and with length of previous tropical exposure.

There was an extensive incidence of skin affections.

It was evident to the authors that the degree of physical deterioration found was quite inadequate to account for the marked loss of general efficiency apparent in the ground crew. Members of the Australian military forces exposed to a physical environment no better than that to which the ground crew were subjected showed smaller loss of efficiency, and this is taken to support the conclusion that physical effects play a relatively small part in causing the deterioration observed. This leads to the conclusion that the major part of the deterioration is due to psychological causes.

The influence of various psychological factors is discussed, and it is remarked that, by attention to sound principles, psychological deterioration can be avoided, or reduced to a minimum, in civilian settlements in the tropics.

T. Bedford

## TROPICAL ULCER

CATRYSE, R. M. Note sur le traitement de l'ulcère phagédénique tropical [The Treatment of Tropical Phagedaenic Ulcer] *Ann Soc Belge de Méd Trop* 1948, Mar 31, v 28, No 1, 1-5, 2 figs on 1 pl

The author treats tropical phagedaenic ulcers by a method based on the technique of Winett-Orr. Under general anaesthesia, for which sodium pentothal suffices, the ulcer is vigorously curetted and the margins excised with curved scissors until a healthy bleeding surface is produced. Compresses of sterile vaseline gauze are then placed on the wound and the whole is enclosed in a plaster-of-paris-case, without window. Seven days later the plaster is removed and the wound is dressed for several days with mercurochrome and sulphanilamide powder, until it appears free from infection. In cases of large and heavily infected ulcers it may be necessary to repeat the curetting and plaster treatment. Finally the wound is covered with skin grafts, which are left undisturbed for 10 days.

The author has treated 41 cases by this method, with successful results in all cases although some of the ulcers were of 15 to 20 years standing.

[Treatment by occlusive dressings, after cleansing and applying sulphamids made powder was one of the methods recommended by the War Office for the treatment of desert sores during the 1930-43 war] H. L. Harnett

CASSELLANI A. Tropicaloid Ulcer (Myxatoid Ulcer Superficial Tropical Ulcer). *Ann. Inst. Med. Trop. Lisbon*. 1947 Dec. v 4 297-312, 14 figs. on 4 pls.

This is an amplified account of that given in the author's recent book on the Diseases of Africa (*Le Maladies de l'Afrique*) published in Rome in 1946. The condition differs in several respects from *ulcus tropicum*, *vellet sore* and other forms of ulcer though resembling them in some points (hence it is presumed, the name "tropicaloid"). Cases were seen by the author in Libya during the late war when he met with it under the names *Marmarica ulcer* or *oasis ulcer*. The causative organism isolated and named by the author is the *Micrococcus microdoides* coccoid forms being 0.6-1 $\mu$  in diameter and coccobacillary forms 0.6-2 $\mu$  long and 0.3-0.6 $\mu$  broad. It is Gram-negative when first isolated but later becomes positive and yet later still returns to the Gram-negative state. It is usually found mixed with other organisms, staphylococci and diphtheroid bacteria. According to the author growth on Italian agar is not profuse and produces no pigment but on Portuguese or American agar a yellow pigment is formed. In liquid media, broth and peptone water growth is scanty. It does not liquefy gelatin. It produces acid in glucose, laevulose, lactose, maltose, saccharose and galactose, but not in mannitol, and no gas is any. Inoculation on the scarified skin of volunteers, or to small wounds, was followed in 10-12 days by typical ulcers which, like the natural ulcers, took 3 months or so to heal, leaving either pigmented scars or infiltrated plaques. Similar inoculation with the associated organisms resulted only in small inflammatory lesions which crusted over and healed completely in 2-3 weeks. The ulcer may be tender on pressure but is not usually painful. There may be one to four of them, usually in the leg, each 1-4 cm. in diameter with a reddish, granulating base and an inflamed periphery, edges not raised or undermined. There is no lymphangitis or corresponding lymphadenitis. Apart from the superficial types, nodular or more infiltrated types are seen and also recalcitrant crusted and pyodermic types. [In his book the author gives in more detail the points in diagnosis between this and other forms of ulcer: *ulcus tropicum*, *vellet* (Barcoo rot), yaws, leishmaniasis, leprosy, myxatoid ulcer, varicose, syphilitic, tuberculous and trophic forms.]

The best treatment seems to be the simple one of rest, basic acid fermentations followed by a dermatol ointment or iodoforn and benzoin. Sulphonamides were tried without much success, but penicillin was more satisfactory in a few cases. The article has some excellent photographs showing the natural condition and that seen in the inoculated volunteers.

H. Harnett Sc.D

# MISCELLANEOUS DISEASES

ALKAY W. J. One Year of Military Medicine in the Central Mediterranean Area. *Acta Med. Orientalia*. 1948 Apr. 7 No 4 76-82.

This is a review of 3,835 patients treated in hospital from July 1945 to June 1946 of whom 1,657 were in two hospitals in Italy (1945) and 2,195 in Greece

(1946). Fifty per cent of these suffered from infectious diseases, all, with the exception of about 250 prisoners-of-war, being young and healthy men. The most interesting groups of cases are described in detail.

The distribution was as follows —

Malaria	Italy	Greece	Total
Benign tertian (primary)	29	18	47
Benign tertian (relapse)	77	9	86
Malignant tertian (primary)	3	—	3
Malignant tertian (relapse)	1	—	1
Clinical malaria	3	2	5
Total	113	29	142

The low incidence of malaria is thought to have been due mainly to suppressive administration of mepacrine. *Plasmodium vivax* infections, as compared with those caused by *Plasmodium falciparum*, appeared to show relapses in a larger proportion of cases after the drug was discontinued, but some of the so-called relapses were probably re-infections. Every effort was made to diagnose cases microscopically before beginning treatment.

**Bacillary dysentery** This was commoner in Greece, the disease being always of a mild type. There were 103 cases. Sulphaguanidine appeared to shorten the illness.

**Amoebiasis** The figure of 67 cases is considered to be too low, as it was found to be impossible in practice to re-examine microscopically every diarrhoea stool, but the need for the most careful investigation of all patients where this infection is suspected is stressed, and sigmoidoscopy was done on all the cases of amoebiasis before discharge. It was found that fresh cases intensively treated from the beginning showed comparatively fewer relapses than the more chronic ones.

**Enteric fever** Six cases were seen, this is striking evidence of the efficiency and thoroughness of preventive inoculation with T A B vaccine.

**Miscellaneous infectious diseases** There were 1,390 cases, the most common were infective hepatitis and "short-term" fevers. The former (240 cases) was usually a mild infection and a number of cases of hepatitis without jaundice were seen. These patients were given a diet low in fat, rich in proteins and carbohydrates, with a minimum of roughage. Of the short-term fevers (472 cases) a large number were typical sandfly fever and only 1 case of dengue was seen. Of 554 cases of respiratory affections, the most interesting group was primary atypical pneumonia (149 instances). There were 106 patients with pulmonary tuberculosis, 45 being prisoners-of-war.

Warnings were given against the use of sulphonamides in eczematous conditions. Psychosomatic disorders (gastro-intestinal, respiratory, cardiovascular and urogenital) accounted for 71, and pure psychoneuroses for 121 cases. Sixty-eight patients were admitted without any definite illness being found but there appeared to be no definite evidence which would label these as malingers.

C. F. Shelton

DAVIES J. N. P. Pathology of Central African Natives. Malaga Hospital Post Mortem Studies—VII. *East African Med. J.* 1948 June v 5 No. 6, 228-35. [20 refs.]

This series which is concerned with causes of death in African children consisted of 164 children under the age of 10 years divided into three groups according to the usual convention.

Group I—Neonates, 28 children under the age of 28 days. The most common single cause of death was infection, mainly pneumococcal. In none of the cases was evidence of syphilis found, nor is malaria reported as a cause of death.

Group II—Infant under the age of 12 months. This group consisted of 44 children. Malaria was a cause of death in only 8 cases. As a direct cause of death it does not appear to be of significance though it may act indirectly by undermining resistance. Only one case of syphilis was observed. Again, infection particularly pneumococcal, was the most common cause of death. Of 6 cases of purulent meningitis four resulted from the pneumococcus. Most of the children showed evidence of malnutrition but in only 3 was it marked and considered a cause of death.

Group III—Children from 1 to 10 years. This group contained 100 children and in them multiple disease manifestations occurred rendering it difficult to determine the exact cause of death. Infection, malnutrition and malaria were often associated.

Malnutrition lay at the background of most cases. Nearly every African in 1948 shows signs of a fine monolobular erythrosis with portal cell accumulation. This suggests that nearly every African child goes through a kwashiorkor phase. The importance of malaria as a cause of death was slight. Infection were responsible for the greatest number of deaths, the pneumococcus being the chief offender and the tubercle bacillus a close second. There seems to be no distinction between childhood and adult tuberculosis in Uganda; all cases seem to show the characteristics of primary infection. Of tropical diseases there were only 9 cases of malaria, 2 of amoebiasis and 6 of plague. There were 11 cases of neoplasms and one of malignant hypertension were noted. Syphilis does not appear in the list of findings and a feature was the unimportance of helminthic infections.

[The paediatrician in Kampala would find that his problem did not lie in the field of tropical medicine but in the cosmopolitan diseases of childhood.]

P. I. Clark

MILAR J. C. A Brief Review of Fifty Years of Medical History in Selangor Federation of Malaya. *Med. J. Malay.* 1948 Mar v 2, No. 3 161-73.

This is an interesting piece of Colonial history compiled, one presumes, from official reports. It cannot satisfactorily be summarized. The author deals with his subject under various heads: hospitals, health legislation, dangerous infectious diseases, prevailing diseases, beriberi, fever and malaria, dysentery and diarrhoea, influenza and enteric fever.

In a table are given the number of cases of smallpox, bubonic plague, beriberi, dysentery, diarrhoea and fevers reported each year from 1897 to 1947. The only one of these I show steady reduction is beriberi which began to decline from figures of 2,100 per annum before the 1914-15 war to 99-444 per annum from 1940 to 1947. Plague was never common and neither cholera nor smallpox was responsible for large numbers of cases.

The author does not give any systematic account of the outstanding investigations made during the period, but rather just opinions (as would be) of our eminent servants medical or lay in their reports. Charles H. Mack

CASIS SACRE, G Impresiones parasitológicas a través del Seguro Social Mexicano [Parasitism in Mexico] *Medicina Mexico* 1948, July 25, v 28, No 560 318-24

The staff of the Social Security Service in Mexico has been inquiring into the existence and prevalence of parasitic infections in the State. The general conclusions are that intestinal parasites are much more common among the poorer and uneducated classes of society and that, in order of importance, these parasites (and infections) are *Enterobius vermicularis*, *Ascaris lumbricoides*, *Taenia saginata*, *T. solium* and *H. nana*, amoebiasis and giardiasis. Malaria, *Trichuris* infection and uncinariasis cases are comparatively few and usually imported.

*Enterobius vermicularis* is the commonest infestation, in Mexico City 80 per cent of the parasitism is by this worm and it is specially common among those living in poor and insanitary conditions and among the larger families. Treatment by gentian violet, in courses of 8 days with a week's interval, proves satisfactory. *Ascaris lumbricoides* is very common also, again among the poor living in insanitary conditions. It is found even in children less than a year old. Hexylresorcinol is the usual drug for treatment, or, if the children will not swallow this, santonin and chenopodium in castor oil. *Taenia saginata* is more frequently met with than *T. solium*, especially in the Federal District. Cases are probably more numerous than is supposed because patients do not come for treatment unless they see the proglottides themselves, and there exists the peculiar belief that expulsion of the worm as the result of medical treatment is followed by serious after-effects, perhaps even death of the patient, they prefer to keep their worms year after year. *Hymenolepis nana* is seen, almost exclusively in children. Filix mas is not used in treatment "in spite of its being recommended in the books because, if this medicament is dangerous for adults, it must be more dangerous for children." The author gives atebryn instead.

Intestinal amoebiasis has been reported as infecting 5 per cent of 105 school-children in a residential part of the capital and in 34 per cent of the inmates of a Children's Home (alumnos de un internado) in the suburbs. How much of this is due to *E. histolytica* is doubtful because, as the author naively states the technical microscopists find it difficult to distinguish *E. histolytica* from *E. coli*. In view of possible liver abscess or other complication, efforts will be made to render the diagnosis more certain and to determine the actual prevalence by examining the faeces of large numbers of the people, by routine examination of the faeces of all patients complaining of diarrhoea or dysentery and "by selecting microscopists whose findings can be received with confidence." Giardiasis is reported as present in 10-20 per cent in Mexico City, atebryn is used in treatment. Malaria is mostly associated with *P. vivax* and is more common than is generally reported because most people regard it lightly and treat themselves, on the other hand, anyone with fever particularly if it is rhythmic (periodic) takes quinine or atebryn or plasmoquine without calling in a doctor, or these drugs are prescribed by the doctor without any preliminary blood-examination.

H Harold Scott

SYMMERS D Splenomegaly. *Arch Pathology* 1948 Mar v 45, No 3 385-409 [37 refs]

A general review

DANARAJ, T J Eosinophilic Lung *Med J Malaya* 1947 June, v 1 No 4, 278-88 2 graphs [18 refs]

Eight cases of this condition are described, the patients being four Ceylonese, three Indians, and one Chinese, all males except one. Symptoms consisted of

1. breathlessness and cough, sputum being sometimes purulent and occasionally blood-stained. Six of the patients complained of loss of weight and in one a Ceylonese schoolboy this was the only presenting symptom. The authors found the most troublesome complaint to be a paroxysmal cough which was always worst at night.

On clinical examination rhonchi were heard scattered throughout both lung fields in five cases the lungs being clear in the other three. X-ray examination showed characteristic mottling of both lungs in four cases and of one lung in one case. Another showed increased vascular markings, while in two the lungs were clear. Sputum was examined for tubercle bacilli and mites but none were found. The technique used for searching for mites is not described. A marked eosinophilia was found in all cases, the highest count recorded being 33,264 eosinophils per cmm.

Treatment consisted of arsenic, given in the form of nearsphenamine six injections of 0.3 gm. in six cases and stovarsol 4 grains t.i.d. for seven and ten days respectively in the other two. Four of the patients were cured three were improved, while one was showing a favourable response although treatment had not been completed.

The author emphasizes the importance of performing repeated blood counts in order to avoid missing this condition. Out of the eight cases which he describes, one had been wrongly diagnosed as pulmonary tuberculosis and three as bronchial asthma. One of the latter had an initial eosinophil count of 4,097 which rose to 17,700 three weeks later.

H. T. H. Wilson

ROSEN, A. P. & SCARLAX, J. J. *Parasit. New England J. of Med.* 1948, Sept. 2, v. 239 No. 10 367-8.

A case of favism in a five-year-old boy is presented with a review of the clinical features. More cases of this syndrome will be seen in the United States because the fava bean is now cultivated here.

8. S. A Case of Mollusca. *India Med Gaz.* 1948, Apr. 83 No. 4 164-7.  
The case occurred in Rangoon.

SIGALAS, R. & PAUTRIFF, R. Sur quatre cas de myiases sous-cutanées à hypodermes les Indes. (Four Cases of Subcutaneous Myiasis due to *Hypodermes*.) *Bull. Soc. Path. Exot.* 1948, 41 Nos. 5 & 6 340-84.

## PROTOZOOLOGY GENERAL

TALLAFERRO, W. H. The Inhibition of Reproduction of Parasites by Immune Factors. *Bact. Reviews* 1948, Mar. v. 12, No. 1 1-17 2 figs. 68 r (1.)

This interesting paper is an exposition of certain views regarding the mechanisms restricting unlimited reproduction in parasites and the part played by them in immunity. Much of the most important work on this subject has been carried out by the author and his summary here of this and of the studies of other in the same field make a very useful contribution to the subject.

It is not possible in a short review adequately to summarize the content of the paper and those interested in the subject must consult the original. But a brief account of the salient points will indicate the scope of the work.

Inhibition or impairment of reproduction in parasites brought about by immunity mechanisms must, in the last resort, depend on the effect of the latter in impairing the metabolism of the parasites

This inhibition of reproduction can be recognized in three forms. The first is exhibited in the case of certain nematodes. Here the immunity mechanism produces its inhibitory effect on reproduction merely as part of a general depression of the metabolic processes of the parasite, but without specific action against reproduction.

In the next form, the immune reaction exercises the same unspecific generalized inhibitory effect on metabolism, including that on reproduction but, in addition, is reinforced by physiological disorganization in the host itself, caused by toxins produced as a result of antigen-antibody reactions. Of this nature is the sum of the immunity responses in malaria.

In the third form, there is a demonstrable and special retarding effect on reproduction, so specific that it leaves the remaining normal metabolic activities of the parasite practically unaffected. This type of inhibition of reproduction is seen in certain non-pathogenic trypanosomes such as *T. lewisi*. The specific antibody producing this effect was described by the author in 1924 and later named "ablastin". It has been the subject of research by a number of investigators.

H E Shortt

VAN CREVELD, S, ARONS, P & DE BRUYNE, J I. Toxoplasmosis gecombineerd met situs inversus totalis [Toxoplasmosis in a Patient with Situs Inversus] *Nederl Tijdschr v Geneesk* 1948, Sept 18, v 92 (III), No 38, 2903-9, 5 figs (4 on pl.)

The English summary appended to the paper is as follows —

"Description of a case of congenital toxoplasmosis in a girl with complete situs inversus. The diagnosis of toxoplasmosis was founded besides on the presence of characteristic clinical symptoms, on the result of serological reactions. A sister of this girl, born 15 months after our patient, is now 8 months old and till yet shows neither clinical symptoms nor serological reactions of toxoplasmosis."

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## ENTOMOLOGY AND INSECTICIDES GENERAL

JAMES, M T. The Flies that cause Myiasis in Man. *U S Dept of Agric Wash Misc Publication No 631* 1947, Sept, 175 pp, 98 figs [160 refs]

This publication provides a general review of the subject of myiasis in man, followed by a systematic consideration of the species of flies involved. It is an extremely valuable general account of the subject.

In the first thirty pages, the author discusses the classification of myiasis, a rather amorphous subject. Patton, as will be remembered, grouped his insects into those of which the larvae are specific and obligate parasites of man (or other vertebrate), secondly those which are semi-specific (normally breeding in dead material but occasionally living in diseased tissues on a living host), and thirdly those of which the larvae occur accidentally in the gastro-intestinal tract (or other passages). Bishopp and others on the other hand have adopted a classification based on the organ or tissue affected. This suits the surgeon, but the entomologist rightly objects, because a particular insect may parasitize several organs and appear in several places in the classification. In the present work, the author uses a rather full classification based on site and organs, but sets out most of his data under genera and species. His general discussion of





provisionally that in one experiment *Dermacentor pictus* induced an immunity in the rabbit, but there was no cross immunity when *Hyalomma detritum* was used

H S Leeson

**CULPEPPER, G H Rearing and Maintaining a Laboratory Colony of Body Lice on Rabbits** *Amer J Trop Med* 1948, May, v 28, No 3, 499-504, 1 fig

A review of the literature indicates that the body louse (*Pediculus humanus corporis*) has not been successfully reared for more than two generations without results obtained in the successful rearing of 25 generations without certain domesticated rabbits

The lice were kept at 85°C (29 4°C) and 60 per cent RH in beakers and Petri dishes, on patches of blue or black woollen cloth approximately 1½ inches square. The patches were transferred to the bare skin of the rabbits, placed on their backs in specially designed stanchions. A photograph illustrates how the rabbits are held. Two feeds a day are sufficient, 1,600 to 4,000 lice can be fed at one time. A colony of 40,000 lice is being maintained on sixteen rabbits, four being used each day.

In initial tests only four out of twenty-five rabbits were found to be favourable hosts, later seven out of ninety-seven were favourable. On favourable rabbits the lice feed to repletion in 12 to 20 minutes, whereas on unfavourable animals the lice attach more slowly and take up to 30 minutes for repletion. By transferring lice of the tenth generation from favourable to unfavourable rabbits a strain was built up which was sufficiently adapted to the unfavourable rabbit to produce a satisfactorily vigorous colony. Lice have been carried through fifteen generations, on unfavourable rabbits, after ten on favourable ones.

Data are given which show that egg production and longevity of rabbit-bred lice compare well with those of lice reared on man, and lice from naturally infested men can be reared on favourable rabbits just as successfully as those from the laboratory colony. There was no difference in susceptibility to pyrethrum and DDT between lice reared on man and those reared on rabbits.

H S Leeson

**BARRY G T & BOYER R The Synthesis and Biological Toxicities of some DDT Homologues and related Compounds** *Canadian J Res Sect B Chem Sci* 1948 July v 26 No 7 511-17 [14 refs]

**VARGAS, L Fototropismo positivo en larvas de mosquito intoxicadas con DDT. [Positive Phototropism in Mosquito Larvae Poisoned by DDT]** *Rev Inst Salubridad y Enfermedades Trop Mexico* 1948, Mar, v 9, No 1, 47-9.

The English summary appended to the paper is as follows — "Mosquitoes *Aedes* and *Anopheles* show in the adult stage, during the excitation period produced by the poisoning with DDT a strong positive phototropism. The same phenomena can be observed in larvae of *Aedes aegypti* and *Anopheles pseudopunctipennis typicus*."

**ENICK, K Die Wirkung neuartiger Insektizide auf Milben I Mitteilung Laboratoriumsversuche [The Effect of the Newer Insecticides on Ticks and Mites]** Reprinted from *Deut Tierärztl Woch* 1948; v 55, Nos 5/6 & 7/8, 40-43 51-6

The author reviews our knowledge of the effect of the newer synthetic insecticides upon ticks and mites (Acarina) and describes his own experiments

In his own work the author used a number of substances which are referred to under proprietary names. In nearly all cases the formula of the actual insecticide is quoted, but the methods of compounding (which may so greatly influence the efficacy of the insecticide) are withheld. The insecticides included DDT, xanthogen, hexachlorocyclobexane, p-chlorophenylchloromethylsulphone and others, also simpler materials e.g. sodium arsenate, phenol etc. The test animals were *Ornithodoros*, *Ixodes*, *Dermatophagus* and *Psoroptes* (causing mange in rabbits). They were exposed for stated periods on impregnated filter paper, but the experimental methods are not fully explained and the dose of material per unit area of paper is not ascertainable.

The results are tabulated, but are difficult to summarize. One observes the great resistance of *O. moubata* to many materials (as already recorded by ROBINSON this Bulletin 1944 v 41 97). It is however relatively quickly killed by hexachlorocyclobexane and E 803 f (diethyl-p-nitrophenyl-monothio-phosphate) the latter is remarkably effective against several other Acarina, but is dangerous to mammals.

P. A. B. Ives

### LABORATORY PROCEDURES

MAXWELL, R. D. & FRIGELSON, P. A Modified Method of preparing the J.S.B. Stain. } Lab. & Clin. Med. 1943, June, v 33, No. 6, 777-82, 1 fig.  
[11 refs.]

A slight modification in the preparation of the polychrome methylene blue of J.S.B. stain is shown to be advantageous. The original method of autoclaving the solution and adding potash to the resultant fluid did not always give constant results. Instead, the mixture of 0.5 gm. of medicinal methylene blue, 0.5 gm. of potassium dichromate and 3 cc. of 1 per cent. sulphuric acid in 500 cc. of water is heated for three hours in a boiling water bath and the precipitate is removed by filtration. It is dissolved in 500 cc. of M/20 disodium hydrogen phosphate and the solution is allowed to mature for 48 hours before use. It keeps well for months, but if required the precipitate may be dried in a vacuum desiccator and dissolved when necessary in the phosphate solution (0.1 per cent. of stain).

It was discovered by spectrophotometric methods that the polychrome methylene blue consisted of a mixture of about 25 per cent. methylene blue and 75 per cent. azure blue. An artificial mixture of these was found to stain nearly as well as the natural product. (The authors use a very acid wash water (buffered at pH 6.7). A more alkaline water (about 7.2) is better if slipping of the red blood cell is to be demonstrated.)

P. C. C. Garnham

### REPORTS, SURVEYS AND MISCELLANEOUS PAPERS

CHRONICLE WORLD HEALTH ORGANIZATION 1943 July v 2, No. 7 137-48  
The International Control of Cholera, Smallpox and Plague. A Note on the First Session of the Expert Committee on International Epidemic Control and the Three Joint OHP-WHO Study Groups on the Perilous Diseases.

The Interim Commission of the World Health Organization set up an Expert Committee on International Epidemic Control "to examine the circumstances

underlying the spread of the major epidemic diseases and to restate the principles which should serve as a basis for their international control" The first session of this Committee in April was preceded by a meeting of three study groups of experts in Paris, set up jointly by WHO and the *Office International d'Hygiène Publique* the groups made observations on recently established facts to be considered in the drafting of new international sanitary regulations

The first group, which dealt with *cholera*, defined "medical examination" as including such laboratory examinations (e.g., rectal swabbing) as are deemed necessary by health authorities They recognized anti-*cholera* vaccination as of definite value but, in view of the relative character of the protection afforded, they felt that vaccinated persons should not be exempted from all control measures They considered immunity to be manifest as early as the fourth day after injection, reaching its maximum on the eighth day and lasting at least six months A single injection of 1 ml of vaccine confers an appreciable immunity and constitutes a proper procedure for mass-vaccination campaigns Two injections at a week's interval are preferable and should be given to those particularly exposed There is no contraindication, as *cholera* vaccination gives little or no reaction, it can be applied to all ages provided care is taken in the case of infants to reduce the dose in proportion to body weight The group also discussed the antigenic potency of the mixed strains used at present and the transformation from "smooth" to "rough" forms during the course of the disease and convalescence The WHO Expert Committee on Biological Standardization will consider these observations in arriving at a definition of a universally acceptable vaccine

The second group discussed *smallpox*, under the headings of the pathogenic agent, modes of transmission and vaccination They recommended new studies on egg media of the agents responsible for mild and malignant forms, which appear to be identical but have not yet been conclusively proved to be so RNET's work in Melbourne on the estimation of immunity was considered essentially valuable and should be repeated On transmission, the group felt that all the possibilities had not been explored and recommended studies on the existence of the virus in bucco-pharyngeal droplets They reaffirmed the fourteen-day quarantine period as laid down in the Conventions Vaccination still remains the outstanding measure of defence The group recognized the superiority of calf lymph and preferred Leake's multiple pressure technique The danger of post-vaccinal encephalitis for a community is not to be compared to that of *smallpox* in the absence of vaccination The best way to avoid this complication was to carry out primary vaccination well before school age Babies should be vaccinated between the third and sixth months In the case of an epidemic, all children, irrespective of age, should be vaccinated

Of great importance are the definitions suggested for the reactions observed after re-vaccination In addition to the successful and accelerated reactions, they define the so-called immunity reaction, for which they prefer the term "precocious non-vesicular" as "characterized by the appearance after the first day, of a vaccinal lesion which does not develop beyond the papulo-macular stage, is pruriginous and disappears at the latest on the third day" It is in reality the expression of an antigen-antibody reaction which does not necessarily imply that it is accompanied by immunity They also recommended that all vaccination certificates which did not record a success or an accelerated reaction should be considered valid for six months only, while a doctor's statement confirming that he had observed a reaction of either kind should be valid for three years at least (The Expert Committee considered that it was impossible to adopt this fundamental change of principle without further study, and deferred a decision)

The group on *plague and other diseases* recommended residual insecticides such as DDT as the chief measure of international protection against plague. The combined use of the new rodent poisons and insecticides should eradicate plague from ports, towns and villages but was not of course effective against zoonotic enzootics. It was recognized that the incubation period, particularly in mild and vaccinated cases, might exceed the six days recognized by the conventions but the new insecticides and the curative action of sulphonamides and streptomycin diminish the chances of secondary contamination of ectoparasites and thus lessen the importance of the length of the incubation period. The incubation period of typhus was considered for practical purposes to be fourteen days rather than the Conventional twelve days. The use of residual insecticides is the essential measure for international protection, as in plague but disinfection as well as disinsection of the fomites was recommended in view of the danger of contamination by lice and flea excreta.

The Expert Committee on International Epidemic Control itself considered all these observations and in addition, recommended (1) a delimitation of the endemic zones of pestilential diseases as a first step towards an attack on endemic foci—the best method of all (2) improvements in the present systems of notifying urgent information particularly by broadcasting (3) the inclusion of louse-borne relapsing fever among the pestilential diseases and (4) the inclusion of cerebro-spinal meningitis, dengue fever, epidemic influenza and poliomyelitis among the diseases for which immediate notification of epidemics must be made.

[Apart from the elimination of endemic areas, the procedures for international protection against epidemics—still known collectively as "quarantine" though quarantine as such now plays but a minor rôle—fall into three stages. First, to collate and agree on the scientific measures required in the light of the most recent knowledge. Second, to translate these requirements into acceptable administrative measures. Third, to put such agreed administrative measures into force by international and national legislative action. The study groups referred to above represent the first of these processes, the Committee on Epidemic Control represents the second, and the third will be the adoption in due course of international regulations by the World Health Assembly in place of the existing Conventions, and their implementation by States members of the World Health Organization.]

Vernile M. Groves

WASHINGTON. DEPARTMENT OF STATE. Fourth International Congress on Tropical Medicine and Malaria. Abstracts. 1948 May 10-18, pp. iv + 148. Washington D.C.

In the past there have been two distinct series of International Congresses of direct concern to tropical medicine—that on Malaria, and that on Tropical Medicine. Both of these had their own permanent machinery which provided among other business for the calling of Congresses at regular intervals but as a result of the war the machinery of both broke down and they were in danger of permanently lapsing. The President of the United States took the initiative of re-assembling, both on his own authority, at a joint meeting under the title of the Fourth International Congress on Tropical Medicine and Malaria, held in Washington from 10th to 18th May 1948. In doing this, the United States Government has been of the greatest service to the science of tropical medicine, a service enlarged and underlined by the Honorable George G. C. Marshall, Secretary of State in an opening address which stressed the concern of his Government to co-operate with others in the promotion of public health in the tropics.

About sixteen hundred persons took part, representative of all countries with interests in the tropics or subtropics, except the USSR. The machinery of the Congresses was re-established, and a proposal was agreed that the two Congresses should in future be amalgamated in one, though the programme arrangements should be adjusted under two Vice-Presidents in harmony with the predominant interest in malaria. The future of these Congresses is thus assured.

The volume under review is a series of abstracts of papers, mostly unsuited to further abstraction. Their general scope is indicated by the Section titles: Research and Teaching Institutes, Tropical Climatology and Physiology, Bacterial and Spirochaetal Diseases, Virus and Rickettsial Diseases, Malaria, Helminthic Diseases, Protozoan Diseases, Nutritional Diseases in the Tropics, Tropical Dermatology and Mycology, Tropical Veterinary Medicine, Public Health, and Medical and Veterinary Entomology.

Any attempt to assess the relative interest and value of some 170 papers must inevitably largely reflect the interests of the majority lay. Without doubt the place at meetings of the section on malaria, incomparably larger than that at any other, showed where the interest of the writer. However, the attending paper and demonstration by H. E. SHORTT on the pre-erythrocytic cycle of *Plasmodium cynomolgi* with the impromptu inclusion of that of *P. vivax*, were of an outstanding importance, recognized by the award to him of the Laveran Prize. The presentation of evidence on the qualities of new drugs, chloroquine, pentaquine, isopentaquine and paludrine, brought out particularly the efficacy of pentaquine in preventing relapses of *P. vivax* (the relapse rate of the intractable Southwest Pacific [Chesson] strain was reduced from 98 per cent to 25 per cent by a single therapeutic course in combination with quinine, and to 2 per cent by two courses) the probable but as yet unverified superiority of isopentaquine, the toxicity of pentaquine which makes it unsuitable for indiscriminate use in full doses without close medical supervision, and the position of paludrine and chloroquine as prophylactics. The general impression gained was that chemotherapeutic research has produced two almost perfect prophylactics or suppressants against *P. falciparum*, and the progress made indicates that the problem of relapsing *P. vivax* infections will eventually be overcome entirely.

Discussion on the control of malaria centred round two main objects, attempts at total eradication of anopheline species and attempts at permanent but constantly recurring control short of eradication by the use of residual insecticides. F. L. SOPER read an important and imaginative paper which brought together information on past schemes for the eradication of *Aedes* and *Anopheles* and from this tried to forecast the possibilities of future work. Briefly, he considers that it is possible to eradicate any species of mosquito which is entirely domestic in its habits, but that the attack on forest-loving species is impossible on their own ground. Thus and other papers gave together a composite picture of widespread application of the two principles which was a revelation to the reviewer. The picture includes the extinction of *Aedes aegypti* from a considerable proportion of the South American continent, eradication or perfect control of anopheline vectors of malaria throughout the whole of Chile, Peru, Venezuela, British Guiana, Italy, Greece, Cyprus, and from large areas of Bombay Province, the virtual though not yet absolute ending of malaria in the United States, and a number of schemes each more ambitious than would have been thought possible ten years ago. The assembly of knowledge on this subject, with opportunities for formal and informal discussion between those concerned would alone have been adequate justification for the Congresses.

Another outstanding feature was the discussion on the use of chloromycetin against rickettsiae, and particularly the account of its use in the treatment of

scrub typhus in Malaya, which clearly showed that the typhus group of fevers can no longer be considered resistant to treatment. The sessions on helminthic diseases were notable for the discussions of the place of Mebexan in the treatment of bilharzia. Many American veterans have returned from the war with infections with *Haemeria bancrofti* which are either symptomless or mainly productive of anxiety states, and this drug has shown marked success as measured by the disappearance of microfilariae from the blood. It was however a matter of common comment that the resultant death of the parent worm often gave rise to a symptom complex which appeared to the patient to represent an exacerbation of the disease. There was much of interest in the Section concerned with Virus Diseases. This was not confined to tropical infections, concerning itself considerably with infectious hepatitis and transfusion jaundice on which some valuable data of direct concern to the surgeon were presented but the discussions dealt at considerable length with tropical poliomyelitis, yellow fever and other diseases. Poliomyelitis has only recently been recognized as a specific tropical problem, but the work presented at the Congresses should firmly establish its place as such. R. M. TAYLOR and MAX THILKER gave an authoritative statement on the epidemiology of yellow fever which included all the recent work on jungle virus and its transmission, and MAURICE PELTIER gave a useful account of the Dakar yellow fever vaccine which is administered by scarification and has now been given to over five million people. The vaccine is approved by UNRRA and its successor WHO.

The many other subjects discussed ranged over very wide fields. The reviewer was specially interested in a paper on Population Problems in the Tropics by T. LYNN SMITH. In papers by G. GIRARD and K. F. MEYER on the place of live vaccines in the prophylaxis of plague, in one by S. S. VONNEY and P. M. WAGLE on the treatment of plague, which showed that streptomycin is outstanding (3.3 per cent. mortality in all cases, 10.7 per cent. in cases which were septicaemic at the start of treatment) and sulphadiazine of great value (4.2 per cent. and 18.1 per cent. in comparable series) and in a paper by C. G. PAYNE on cholera vaccines. Other readers would, however inevitably select other papers as of special concern, and no one could participate in the Congresses without finding that almost all branches of tropical medicine were enriched both by papers and by formal and informal discussion.

The volume under review consists of about 170 authors abstracts of all varying length and detail, study of which gives little indication of the relative value of the papers. It was useful in arranging one's daily programme at the Congresses and will be of use for record purposes. The reader interested in the substance of papers is advised to wait the publication of the Proceedings which may not be long delayed.

G. Macdonald

THURGOOD W. A. R. *African Medicine. Practitioner* 1948, Sept. & 1949  
No. 903 218-10

In this short paper which records impressions made during a tour from Cairo to the Cape in the space of two months the author makes a few pertinent observations, the first of which is that in Africa, men and money have never been available to allow of systematic surveys of disease such as are now considered essential in any well-run state. Hospital records are inevitably unreliable and the true incidence of disease can only be assessed by survey work. (This observation, no doubt is true but surveys have been made in Africa, sometimes on a large scale though more are needed.) The second is that little is known of the nutritional status and physiology of the "normal" African.

The author refers to overcrowding in hospitals and to the fact that in most medical laboratories there is so much routine work to be done that the opportunities for research hardly exist. He mentions malaria, sleeping sickness, schistosomiasis, amoebiasis, tuberculosis and leprosy as diseases of major importance, and ends by pointing out the valuable work done by members of the Colonial Medical Service.

*Charles Wilcocks*

LEITE, A S, DA LUZ, J V B & DE MEIRA, M T V. Relatório da Missão Médica do Instituto de Medicina Tropical a Angola em 1945 [Report of the Medical Mission of the Angola Institute of Tropical Medicine, 1945] *An Inst Med Trop* Lisbon 1947, Dec, v 4, 465-500, numerous figs on 33 pls (1 coloured) & 1 folding map

The object of this mission was twofold. To verify the presence of dermatomycoses in the Luanda-Malanga region, between Benguela and the Belgian Congo, and, if possible, in the Zaire basin, secondly, to collect material for study and demonstration at the Institute. A sketch map indicates the route taken, by ship, aeroplane and automobile.

The authors found that superficial mycoses were common—pityriasis versicolor, tinea, epidermophytoses at times severe like tokelau (*Tinea imbricata*), favus, infections by *Trichophyton ferrugineum* (a very fine coloured plate depicts the growth of this on Sabouraud glucose) and other trichophyta, and sporotrichosis.

As regards the second objective, the usual collection was made of helminths, especially schistosomes and their vectors, larval and adult forms of diptera, blood specimens for trypanosomes, microfilariae and spirochaetes. Records are given of cases of leprosy, keloid, gangosa, yaws, late syphilis with mutilations, ulcers, onchocerciasis, etc. The whole account is well illustrated with photographs of the mission and its equipment, very realistic reproductions of favus and sporotrichosis, keloid and fungus affections of the feet.

*H Harold Scott*

HEISCH, R B. A Survey at Garsen. *East African Med J* 1948, May, v 25, No 5, 220-24, 1 map

Garsen is on the Tana River in Kenya, not far from the coast, and was a possible accessory site for the East African groundnuts scheme. A parasitological survey of the indigenous inhabitants was made in 1947. The malaria parasite rate in children was 53 per cent, in adults 9 per cent, the species being predominantly *P. falciparum*, though three infections with *P. malariae* were observed. Nomadic tribes (Galla) showed a high spleen rate (34 per cent), a condition attributed to poor immunity. Night blood films were examined for microfilariae and 4 per cent of the non-nomadic people were found to contain them. Faeces contained ancylostome ova (11 per cent), *Ascaris* ova (15 per cent) and *E. histolytica* (1.6 per cent). *S. haematobium* was frequently seen in the urine (52 cases, but the total examined is not given).

*Anopheles gambiae* appeared to be the vector of malaria, it occurred in large numbers after the long rains in May. *A. funestus* was rare. A tree hole survey revealed the presence of *Aedes aegypti*, *Aedes simpsoni* and *Aedes metallicus*, and various species of the subgenus *Diceromyia*. The commonest and most voracious mosquitoes of the district were *Taeniorhynchus*, one of which (*T. africanus*) was found infected with a filaria.

*Haemophysalis* sp. was found in the blood of local pigeons.

[See also this *Bulletin*, 1948, v 45, 671 for a survey of Taveta by the same author.]

*P C C Garnham*

DE MEIRA, M. T. V. NOUEIRA, J. F. P. & SIMÕES, T. O. Relatório da Missão de Estudo do Instituto de Medicina Tropical a Cabo Verde em 1946-1947. [Report of the Investigations of a Mission of the Institute of Tropical Medicine, Lisbon, to the Cape Verde Islands, 1946-47.] *An. Inst. Med. Trop. Lisboa*, 1947 Dec., v. 4 657-711 41 figs. (4 maps)

The Institute of Tropical Medicine, Lisbon, sent out a team, with Dr Manuel de Meira at the head whose aim was "to carry out studies, clinical, entomological, etc., to acquire knowledge of the pathology of the colony and its characteristic endemic conditions." The same general lines of investigation were followed in the three islands of the archipelago, Sal, Boa Vista and S. Nicolau. The Mission stayed for 7 days in the first-named, 18 in the second and a month in the third. The examinations made and the numbers of persons examined in each of these were small and are not of general interest, but one or two points call for remark.

In the island of Sal there was an outbreak of yellow fever in 1873. Infectious beans, introduced from Brazil. Some 300 persons were attacked, with a fatality of 51 per cent. Whether it exists now cannot be stated with certainty. If isolated cases do occur they are mild and may pass unnoticed among cases of malaria. The determining immunity test has not been carried out. In Boa Vista comparatively few examinations were made. Only 83 were examined for intestinal parasites. 238 were examined clinically and among the only morbid conditions with double figures were diarrhoea, 74 (cause not stated) and chronic bronchitis 18. Noteworthy is the fact that albinism, partial or total, occurred in ten members of a family of 20. In S. Nicolau the number examined was greater. 1,673 specimens of blood were taken for examination later. 294 by day and by night for microfilariae. 10 only for malaria parasites. 494 faecal examinations of 47 persons, by the Willis technique showed *ascaris* to be the most common infestation among those who had never been away from the island and *Trichuris* the next. Hookworm was common in those coming to S. Nicolau from elsewhere especially those recently arrived from S. Thomé. Nineteen cases of tinea were found & due to *Mic. poronifidum*. *Trichophyton ferrugineum* was not found in S. Nicolau. Fungus infections of the feet (tinea) foot were far from uncommon. Figures are not given merely the statement *com. dist. (hand/feet)*. Information is given about the mosquitoes found. [See also p. 1122.]

H. Harold S. G.

CLARKE, M. C. The Blasians of North Borneo. *Med. J. Malaya*, 1948, Mar., v. 2, No. 3 179-83, 1 map.

The Blasians are sea-going Mohammedans who during the past 80-100 years have spread from the Philippines to some of the islands off North Borneo. They are independent, wild and carefree people who do not work for wages and who do not trade anything but small quantities of fish. They are very poor and live in primitive conditions. During the war they suffered considerably at the hands of the Japanese.

The author gives medical information which he collected on Sulu, Island in May 1947. Malaria is common (pleen rat 95 per cent) with anaemia only.

Few adults could be examined they showed *Plasmodium* in the blood. The chief vector in N. Borneo, *An. kribia leucostictus* was found also in this island, breeding in the only two existing swamps in use the water was brackish.

The diet of these people is poor. Fish is an important food, with tapanas and sagu but practically no vegetables and little fruit (part from coconut) are eaten and cause a good much needed. Signs of malnutrition are common—dental caries, bleeding gums, as well as tetanitis, magenta tongue, scurvy.



## Book Reviews

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of the skin, depigmentation of the skin Apart from malaria there is not much actual disease, but the poor condition of these people is largely the result of malnutrition, which could be corrected by introducing vegetables and fruit trees, particularly bananas

Charles Wilcocks

MEYER K F The Animal Kingdom, a Reservoir of Human Disease Ann Intern Med 1948 Aug, v 29, No 2 326-46 [34 refs]

PEARSE, A S [Edited by] Zoological Names A List of Phyla, Classes, and Orders Prepared for Section F American Association for the Advancement of Science 3rd Edition 24 pp 1948 Durham, North Carolina

The second edition of this list [see this Bulletin, 1948, v 45, 216] contained many errors, and was not made available to the general biological public This third edition has been corrected

Charles Wilcocks

## BOOK REVIEWS

WILLIAMS, Ernest [CMG, CIE, MD, FRCS (Edin), etc] Manual of Leprosy pp viii+208, 70 figs (10 coloured) 1948 Edinburgh E & S Livingstone Ltd, 16 & 17 Teviot Place [17s 6d]

This small practical book records the latest conclusions of the author based on his long experience in India and while on tours in Africa and other countries as medical secretary of the British Empire Leprosy Relief Association It is on similar lines to his manual published some two decades ago in India, but is a new and up to date account written for the guidance of "doctors, nurses and lay workers" It deals mainly with a clinical description of the disease and its treatment and preventive measures now in common use, and makes no pretence to be a complete account of all aspects of the subject For this reason the history, bacteriology, mode of infection, prevalence and rates of incidence are dismissed in the first seventeen pages, and are followed by short sections on tissue reaction and resistance and the lepromin test The various recent systems of classification are briefly considered and that of the Pan-American Congress of 1946, based on histological findings, is adopted and summarized in a convenient table under lepromatous, uncharacteristic and tuberculoid types although the difficulties of most workers in leprosy areas in obtaining facilities and time for such histological examinations are recognized by the author

The next few chapters are devoted to a careful clinical description of this protean disease, which is well illustrated by the author's photographs of cases and of histological changes, a few of which are in colour This constitutes the most useful section of the book and it includes eye and other complications, bacteriological examinations, differential diagnosis, case taking and prognosis Thirty pages are next devoted to treatment on the lines advocated by the author, who first recommends the use of injections of hydnocarpus oil and ethyl esters, although in recent years much of the oil supplies to Africa and elsewhere have arrived in a rancid condition unsuitable for this use The active and convenient sodium hydnocarpate (in the form of alepol) is not mentioned, although its use in Calcutta thirty years ago first demonstrated the value of injections of active preparation of these oils A chapter on sulphone treatment records the great advances obtained from their use in resistant advanced lepromatous cases by American workers and by the author himself in Trinidad The recently used sulphetrone is considered to be the most active of these preparations

The last section deals with the method now in use in anti-leprosy control without going into the history of compulsory segregation, which is recommended for the infective cases. The importance of separation of healthy children of infected patients is emphasized. This book can be recommended for the use of workers in the numerous endemic area of leprosy.

L. HIGGINS

DE SOUZA ARAUJO Heracles-Cesar [Chefe da Secção de Bacteriologia e do Laboratório de Leprologia do Instituto Oswaldo Cruz. História da Lepra no Brasil. Vol. II. Período Republicano (1889-1946). Album das organizações antileprosas. (History of Leprosy in Brazil.) pp. xx and 390 pls. 1948. Rio de Janeiro: Imprensa Nacional.

This handsome volume depicts the organizations dealing with leprosy in Brazil during the period 1889-1946, the Republican Period. It is the second volume of Professor de Souza Araujo's epochal work on Leprosy in Brazil and truly a monument of industry. The whole is to be completed in 3 volumes. The first was reviewed in this *Bulletin* last year (1947 v. 44 p. 80). This the second volume is an album of photographs with a minimum of letterpress. In addition to portraits of celebrities there are more than a thousand pictures on 390 plates. One cannot in words review a picture gallery: one can only point out the objects aimed at and indicate their importance. True appreciation of their value can only be attained by personal study of them.

There are in Brazil 38 *Leprosarias* and another under construction in Bahia. Minas Gerais has six, São Paulo five, Pará three and several States have two. The number of patients interned at the end of 1946 totalled 20,638. There are 27 *preventoria* for children and one more in Acre Territory being constructed. Minas Gerais has four, São Paulo three, others have two or one each, with its Director and Leprologist and 15 of them have a paediatric also on the staff.

The volume contains portraits of scientists and administrators engaged in leprosy and its prevention and also photographs of various *leprosarias*, *preventoria*, plans and patients referring to the last decade of the nineteenth and the first 46 years of the twentieth centuries. In addition, there are group photographs of conferences, congresses and festivals. Each State and the various districts are taken in turn and there are collections of photographs of patients, children and institutions of the highest interest. The original idea was to interpolate these pictures and photographs in the text, dividing them into the three phases into which the "Republican period" naturally falls: first to 1920 or the period before modern prophylactic measures were in force; second, the following decade or phase of Inoculation for Prophylaxis by the D.N.S.P. (*Departamento Nacional de Saúde Pública*) the National Department of Public Health; third, the Getulian Period that is the period of intensification of prophylaxis under the guidance of Dr. Getúlio Vargas 1931-1945. It was however found impossible to carry out the plan of producing text and photographs together and the author has therefore brought out this volume of photographs separately, the letterpress forming, to them is to make the third volume which, says the author, is already in an advanced stage.

Professor de Souza Araujo has taken the greatest pains to make the work complete. The reproductions are wonderfully clear and the whole constitutes a collection worth of a place in any library and anyone possessing a copy is indeed to be accounted fortunate. Professor de Souza Araujo is performing a work which will earn him the gratitude of all leprologists and those engaged in the study of the disease and its prevention.

Apart from the intrinsic value of the work itself attention must be drawn to the very generous gesture on the part of the author who is handing over the proceeds of the sale of this volume as he did in the case of the first, to

the International Leprosy Association—an act of philanthropy worthy of the highest honour and gratitude  
H Harold Scott

KEFFER, Luiza. *Índice Bibliográfico da lepra 1500-1943* Vol I A-H [Bibliographic Index of Leprosy] pp xxxviii+1-674 1944

— *Índice Bibliográfico de lepra 1500-1944* Vol II I-P pp xxi+675-1434 1946

— *Índice Bibliográfico de lepra 1500-1945* Vol III Q-Z pp xxiv+1435-1936 1948 Biblioteca do Departamento de Profilaxia da Lepra do Estado de São Paulo—Brasil

This monumental work in three volumes and covering over 1,900 pages has been edited by Luiza Keffer, Librarian of the Leprosy Prevention Department of the State of São Paulo, Brazil

It is the fruit of ten years' constant labour in an institution which has collected "one of the greatest specialized bibliographies in medicine, which, at present, has more than 100,000 cards"

Each work mentioned is to be found in the library of the Department and although the Index is restricted to papers contained there, it is stated that it contains "practically everything that has been written about the legendary disease" Indeed this claim would seem to be well-founded, for the references date from the year 1500 to the present day they are arranged alphabetically and there is a comprehensive system of cross references, so that a given work appears under a number of headings

The editor of the Index appeals again to medical workers and editors to send their special publications to the library, where they shall have the widest international publication it is added that the library deals with no less than 185,000 consultations by correspondence annually It is proposed to organize an Annual Supplement to the Index, which will be published as a special number of the *Revista Brasileira de Leprologia*

The worker interested in leprosy and its history could ask for nothing fuller than this tremendous, carefully prepared and well-produced compilation

H J O'D Burke-Gaffney

CRAIG, Charles Franklin [M D, M A (Hon), D Sc (Hon), F A C S, F A C P, etc] *Laboratory Diagnosis of Protozoan Diseases* 2nd Edition 384 pp, 56 figs & 7 coloured pls 1948 London Henry Kimpton, 25 Bloomsbury Way, W C 1 [27s 6d]

Colonel Craig is one of the leading authorities on tropical medicine in the United States He retired some years ago from active teaching, but returned to fill gaps during the war and has continued to maintain his influence on parasitology in the United States by his contributions to the literature, especially to the literature on parasitological technique

The first edition of this book was published during the recent war and was in great demand amongst medical men in the Forces whose previous experience of parasitology was often very limited The author now feels that, with the many men returning from service who will have tropical infections, especially chronic amoebiasis and malaria, there should be a demand for another edition of his book.

Undoubtedly, Col Craig's long suit is the intestinal protozoa and in particular the amoebae He has made some outstanding contributions to this subject and it is not surprising that he has devoted over two-fifths of the book to amoebiasis and the flagellate infections of the bowel The one hundred and

The last section deals with the method now in use in anti-leprosy control without going into the history of compulsory segregation, which is recommended for the infective cases. The importance of separation of healthy children of infected patient is emphasized. This book can be recommended for the use of workers in the numerous endemic areas of leprosy.

L. A. 73

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Undoubtedly, Col Craig's long suit is the intestinal protozoa and in particular the amoebae. He has made some outstanding contributions to this subject and it is not surprising that he has devoted over two-fifths of the book to amoebiasis and the flagellate infections of the bowel. The one hundred and

forty-five pages on the subject give much more than the student will require and constitute a valuable source of reference for the advanced worker since for example he has given about 20 different media and methods of cultivation of *Entamoeba histolytica*. Three methods of his own are included. He naturally prefers his own methods but in summarising this subject he says that it is better to persevere with one type of medium and perfect one's own technique rather than to try a succession of media. It is somewhat surprising that he has made little reference to the recent work of REES and his colleagues at the National Institute of Health on the cultivation of amoebae with single strains of bacteria this *Bulletin* 1948 v. 43: 55 and 1948 v. 45: 60 and the work on the addition of extracts of heat- and otherwise, killed bacteria. Twenty-five pages are devoted to the complement fixation tests (C.F.T.) a subject which is very much *sub judice* still although the author has been working on it for at least two decades. He is almost the only worker who has had consistently successful results with his own methods. He finds the test positive in the case of the "symptomatic" carrier and whenever he has encountered a positive result he has usually been able to demonstrate *E. histolytica* cysts in the stool after repeated examinations. It is not clear whether he followed up the negative cases quite as assiduously. He considers that the method of BOZICEVIC, HORRIG and WALSTON is less satisfactory since it usually gives negative results in the case of carriers. It would be interesting if this question of the C.F.T. in amoebiasis could be settled since its importance goes beyond that of a diagnostic aid. If in fact the C.F.T. is constantly positive in the case of "carriers" it does indicate that there is some tissue invasion in all these cases (the author's view) but if the test is frequently negative it suggests that in many of these cases there is no tissue invasion (the reviewer's opinion).

The author gives a useful critique of diagnostic methods. He considers that the second stool after saline purgation is more likely to contain active amoebae. In the search for cysts he considers that repeated examinations are necessary and recommends the zinc-sulphate centrifugal flotation method with iodine or haematoxylin for staining. He points out that by direct smear examinations less than 1 in 5 individuals will be identified at a single examination and that 10 will have to be negative before a reasonably certain negative report can be given, whereas by the flotation method one in three or four will be positive. He considers that sigmoidoscopy should not be employed as a routine as only rarely will it help in diagnosis when the examination of the stool is negative. [This will come as a rather a shock to his modern military school who use the sigmoidoscope as lightly as they use a spatula. The real place of the sigmoidoscope is somewhere between these two extremes.]

Part II (50 pages) is on the laboratory diagnosis of the leishmaniasis. The author gives a very complete and accurate account of this. The main criticism offered is that he has given too many methods and even in his critique of diagnostic methods he has simply repeated what he has said before and has not faced the practical side and given a lead to the worker by indicating when and where the various tests should be used. For example he says "The serological tests employed in the diagnosis of kala-azar are all useful but the most valuable are the complement fixation test, the albumin test of Nagler and the antimony tests of Chagas." The C.F.T. can only be carried out in a well equipped laboratory whereas the albumin test can be done in any dry-gas jar where there is a test tube and a bottle of formalin. The latter however has very definite limitations and is very little used in the first three months of the disease. Further in hospital practice, the parasite should always be demonstrated by smear examination or by culture. These facts are not clearly explained. Again it is stated thatternal puncture is safer than leishman puncture and is certain a diagnostic method. About the former he states

"serious consequences have not been reported", whereas in fact a number of deaths have been reported, and today few experienced workers will agree that it is as certain a diagnostic procedure, though it was fashionable to say so ten years ago. On the subject of peripheral blood cultures, he quotes Knowles as having reported only one positive culture in twelve cases of kala azar. The reviewer does not know where he encountered this statement, but it must have been in a paper written in Knowles's early days, since later he looked upon culture of the peripheral blood as a very reliable method, if the technique was right.

Part III (53 pages) is on the laboratory diagnosis of the trypanosomiasis and Part IV (8 pages) on that of coccidiosis. Part V (90) is on the malarial plasmodia. This is an informative chapter, it includes 6 coloured plates of which three are of the thick-film appearances of malaria parasites taken from Aimee Wilcox's useful manual. There are seven pages devoted to the flocculation tests in malaria which the author takes rather more seriously than do most workers in this field. The last few pages (Part VI—8 pages) are devoted to balantidiasis.

It is a book of limited scope which medical parasitologists will find very useful for reference.

*L. E. Napier*

RICHARDSON, Ulick F. [B Sc., M R C V S] *Veterinary Protozoology* pp viii+240, 1 coloured pl & 34 figs. 1948. Edinburgh: Oliver and Boyd, Tweeddale Court & London: 98 Great Russell Street, W C. [18/-]

This is the first textbook, so far as the reviewer is aware, to be published in this country dealing exclusively with veterinary protozoology. It consists of some 250 pages and is divided into twelve chapters, the first of which is an interesting general survey of the protozoa affecting man and domestic stock, and deals with the structure, classification and reproduction of the parasitic protozoa as well as with their pathogenicity, the course of the diseases they produce and the immunity or tolerance which sometimes follows such infections. Chapters II–X, which cover 155 pages, are devoted to a systematic description of the various species of pathogenic protozoa and their life-cycles, together with an account of the methods to be adopted for their control and for their eradication from the host. Chapter XI, consisting of 21 pages, is devoted to chemotherapy, although, as previously stated, the treatment of infections due to particular species of parasites is dealt with in the preceding chapters. The twelfth, and last, chapter is an excellent account of the techniques to be adopted for obtaining, examining, and preserving pathological material. At the end of each chapter there is a useful list of references, but many of these are of considerable antiquity. This quoting of work, once of fundamental importance, but now altered by the addition of more recent knowledge, occurs elsewhere in the text, and it is a little surprising to find such statements as (p. 74) 'it has recently been found (Brumpt 1937)', and (p. 127) 'recently attempts have been made by Schilling (1936)'. The reviewer has noticed a few slips in spelling, as (p. 89) 'Louri', and (p. 66) 'Maure's dots'.

The author in his preface states that 'this book has been written in the hope that it may be of value to veterinary students, and to workers in the tropics, where protozoan diseases are the principal problems of the veterinary surgeon, and the chief obstacle to stock improvement'. It is also hoped that it may stimulate interest and lead to research work, which will benefit both veterinary and human medicine. The reviewer has no doubt that the book will stimulate interest in veterinary protozoology to which human medicine already owes so great a debt and it will prove helpful to workers in the tropics, but he has grave misgivings as to the wisdom of using it for the instruction of the inexperienced undergraduate or newly qualified practitioner. The reasons for

these misgivings arise from the fact that the author sometimes presents the matter often without comment with a series of views, one or more of which are at variance with the remainder. In addition, he sometimes gives opinions unsupported by convincing evidence which are in conflict with existing belief. The following may be cited as examples of contrasting statements quoted without comment. Having given an account of the life-cycle of *Plasmodium falciparum* including its development in the intestine of the tick, the author on the same page quotes RITCHIE (1936) as saying that there is no development of *Plasmodium* in the intestines of ticks. Method for the control of *T. parva* (p. 56) occupies three pages and the author having described control by hygienic, then gives two other methods. "All animals in the infected herd are examined daily and any showing fever are slaughtered, the herd being moved to a clean area three times at intervals of fifteen days." Having mentioned reasons for this method and recommended that the area should not be restocked with cattle for eighteen months, he continues: "a more drastic method which has met with more success is the slaughter of the whole infected herd, and the abandonment of the grazing ground for cattle for eighteen months." While on the same page under Immunization, he describes the classical TUITER (1917) method as follows: "Loses were occasionally heavy up to 30 to 40 per cent, but far less severe than if the disease had spread unchecked. The method does not appear to have been used with success elsewhere. Many similar examples particularly as regard treatment might be quoted from other chapters. To the worker with considerable knowledge of or access to modern literature such divergent opinions are stimulating and interesting, but to the inexperienced student section, immediate information they are confusing and depressing.

The following may be given as examples of statements at variance with existing beliefs when describing the life-cycle of the malaria parasite in man: the author writes (p. 62) "the parasite is a minute uniloculate organism which enters the blood stream and forces itself into a red blood corpuscle where it increases in size and becomes rounded off." Continuing with the malaria parasite he states (p. 67) "not only are parasitized erythrocytes destroyed but also enormous numbers of unparasitized cells and it may be that the pigment also acts as a haemolytic, and on the same page it has been stated that a mononucleosis in 15 per cent or more is diagnostic of malaria. His views regarding the transmission of leishmaniasis are similarly worthy for—

the leishmaniasis of the dog may be transmitted by species of *Phlebotomus* not only *P. perniciosus* and *P. papatasi* and by the tick *Hyalomma marginatum* and also probably by fleas" (p. 95).

The violence of a falciparum stage of trypanosomiasis is discussed at some length and the author would appear to believe that such a stage exists (p. 103) "this is not the generally accepted view while the former view is now supported by evidence to support the statement on page 101—It is thought that the late development of the trypanosome at the time of infection may influence the infection rate and that for instance no infection with *T. brucei* might occur if no stumpy form were present in the blood. Two other chemotherapy which might be mentioned are (p. 200) Pentamidine has not yet had satisfactory results in any infection and on page 128 "In human sleeping sickness the drugs which have tested the best for the treatment are antitrypanosomal (ermarmin) and trypanarsole. It is generally agreed that pentamidine has become well established for the treatment and prophylaxis of *T. brucei* in man while although trypanarsole has tested the best of those against *T. gambiense* it has not been so successful against *T. rhodesiense*."

The author will appear well to treat the subject with the exception of the following in common terms for the main part in descriptive terms.



## Book Reviews

Vol 45, No 12]

Mr Richardson's book, which is published at the reasonable price of 18s, should have a considerable sale among veterinary practitioners, as it contains much valuable information which was previously only obtainable by searching through numerous more general textbooks

R M Gordon

BENBROOK, Edward, A [V M D, Professor and Head of the Department of Veterinary Pathology, Iowa State College] & SLOSS, Margaret W [B S, D V M, M S] **Veterinary Clinical Parasitology** 187 pp, 247 figs 1948 Ames, Iowa The Iowa State College Press [\$4 50]

The purpose of this book, as stated in the authors' preface, is "to assist in the diagnosis of parasitism and of parasitic disease by means of laboratory techniques, and to show by illustrations the more commonly encountered forms as well as some of those less often seen."

It is concerned primarily with veterinary parasitology and only three of the more important groups of parasites, namely intestinal parasites, parasitic mites and ticks are considered in the present volume. It is stated that if there is a demand for additional chapters, they may be added when sufficient material becomes available, and, to this end, the book is bound in loose-leaf form, so that pages may be added or moved.

The book covers 187 pages of art paper and some 120 of these are occupied with excellent photographs of specific parasites and illustrations of technical methods. The former are clearly marked on each page showing the animal host to which the parasite refers, and this covers a wide range. Seven pages of photographs are given to intestinal parasites of man. Nine pages show illustrations of pseudoparasites or spurious parasites, a most useful guide to microscopists.

The text deals with technical methods in the greatest detail and illustrates the stages of them with very clear photographs. In the second chapter (dealing with mites) and in the third (lice) lists of species and their hosts are also given. The descriptions of methods of stool examination include the smallest details.

There are no less than 20 pages of references, dealing separately with each of the three chapters, and a most comprehensive index of 10 pages. The work is beautifully presented and produced and contains much that the medical parasitologist will find of practical value. It is indeed an excellent book to have on the bench in any parasitological laboratory which deals with the relevant subjects.

H J O D Burke-Gaffney

NAUCK, E G, with ENIGK, K, VOGEL, J, REICHENOW, E, WESTPHAL, A & WEYER, F **Tropical Medicine and Parasitology** Fiat Review of German Science, 1939-1946 253 pp, 8 figs 1948 Published by Office of Military Government for Germany, Field Information Agencies Technical, British, France, U S

The term FIAT is an abbreviation for Field Information Agency, Technical, and the present volume forms one of a series which, in addition to medicine, deals with physics, chemistry, mathematics and sciences of the earth.

Well then might it be termed a "Review of Reviews" serving to inform the world of research work on Tropical, Medicine, Hygiene and Parasitology during the war years—from May 1939 to May 1946. This has been accomplished by the co operation of many German contributors, who have furnished the contents while the whole has been prepared for publication by the scientific branches of FIAT. Thus the section on general Tropical Hygiene is by E G NAUCK, on Parasitology by E Reichenow and F WEYER Tropical Diseases

of Man are dealt with by NATOK, REICHENOW, VOGEL, WESTERHAL and WEYER, those of domestic animals by H. ENIGK. So condensed is the material that it becomes difficult to convey an idea of the amount of information that this publication contains. Those who look for a detailed account of important investigations do so in vain, but every page gives the impression of enthusiasm for knowledge against adversity. The opening pages are indeed a syllabus of the more important German books on tropical medicine and hygiene as well as of the journals devoted to this subject. The best known of these—

*Zeitschrift für Schiffbau und Tropenhygiene*—was, on completion of the 45th volume in 1941 renamed "*Deutsche Tropenmedizinische Zeitschrift*" but on account of war restrictions, it too in June 1944 came to an end and with it the old spirit of enquiry appears to have been temporarily extinguished. A considerable space is devoted to the subject of acclimatization in the reference to the question of housing and nutrition. The parasitological section, mostly by REICHENOW, affords a detailed review of protozoology in these war years most of which has found its way into the pages of this *Bulletin* and of course includes the original studies of KILUTH, REICHENOW and MUDROW on the erythrocytic cycle of *P. falciparum* and *P. malarium*. Other chapters again summarize work done mainly on therapy upon malaria, blackwater fever, leishmaniasis, trypanosomiasis, amoebiasis, spirochaetoses and bacterial diseases, including leprosy and plague. The virus and rickettsial diseases and tropical worm infections also receive attention and there is a contribution on nutritional disorders. The volume is well documented and should continue to serve as a record of hard-won achievement for many years to come.

P. MANSWORTHY

### LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE

The Langley Memorial Prize which is open to competition among Bachelors, past and present, of the West African medical departments has been awarded to Dr D. G. FITZGERALD MUIR for his essay on Nutritional Eye Disease and Effects of Nutritional Retrobulbar Neuritis.

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Bart	"	Bartonellosis
BL	"	Blackwater
B.R.	"	Book Review
Chl.	"	Cholera
Def Dis	"	Deficiency Diseases
D	"	Dengue and Allied Fevers
F	"	Dermatology and Fungus Diseases
Ent	"	General Entomology
Epid	"	Epidemic Dropsy
Haem	"	Haematology
Heat Str	"	Heat Stroke and Allied Con- ditions
Hel	"	Helminthiasis
Lab	"	Laboratory Procedures
Leish.	"	Leishmaniasis

Lep	signifies	Leprosy
Mal	"	Malaria
Misc Dis	"	Miscellaneous Diseases
Oph	"	Tropical Ophthalmology
Pl	"	Plague
Prot	"	General Protozoology
Rab	"	Rabies
R F	"	Relapsing Fever and other Spirochaetoses
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Sp	"	Sprue
Tryp	"	Trypanosomiasis
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